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BULLETIN ON NARCOTICS

Vol. X, No. 2, APRIL-JUNE 1958

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Bulletin on NARCOTICS

Vol. X, No. 2, APRIL-JUNE 1958

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Some Recent Advances in the Chemistry of the Opium Alkaloids

By David Ginsburg
Department of Chemistry, Israel Institute of Technology, Haifa, Israel

The first review article in this series was published in the *Bulletin on Narcotics* last year and covered work which was published in the chemical literature through 1956 (1).

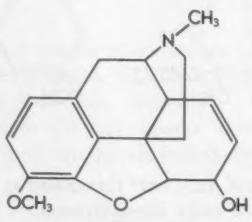
The year 1957 has brought to the attention of chemists interested in the chemistry of the opium alkaloids a number of important papers. The three important contributions described below may be divided into several types : (*a*) a paper which promises much in that it is the beginning of an investigation into the fate of morphine and codeine in the body; (*b*) a series of papers which is the culmination of a very difficult structural elucidation; (*c*) a continuation of the practical synthesis of potential analgesic compounds.

I. *Degradative Studies directed towards the Synthesis of Labelled Morphine Derivatives*

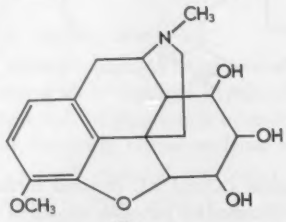
The fate of morphine and codeine in the human body has been the subject of much speculation, but to the knowledge of this reviewer no systematic organic chemical work has been undertaken heretofore in order to determine the identity of possible metabolic products of these alkaloids. It is therefore good news that a master in the field of the opium alkaloids has undertaken preliminary research directed towards the study of morphine and codeine metabolism.

Rapoport, Chadha & Lovell (2) have studied the selective oxidation of the double bond in ring C of codeine and some of its derivatives. The aim was to cleave ring C and then to reconstitute it after replacement of one of the carbon atoms with radioactive carbon which might then permit tracing the metabolic fate of the reconstituted compound. At the same time, ring C glycols may be by analogy with cases known from other fields of organic chemistry and biochemistry (e.g., certain polycyclic hydrocarbons), metabolic intermediates in the biological degradation of codeine or morphine.

Codeine (I) was oxidized to the corresponding glycol (II) by means of osmium tetroxide at room temperature in ether solution and in the presence of pyridine. The resulting osmate was best cleaved by using ethanolic sodium sulfite, the over-all yield of the glycol being 60%.

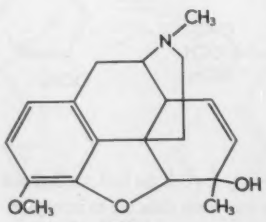


I



II

Similarly, 6-methylcodeine (III) gave the glycol (IV) in 52% yield. Codeinone dimethyl ketal (V) gave its corresponding glycol (VI) in 38% yield and Δ^7-desoxycodeine (VII) gave the glycol (VIII) in 92% yield.



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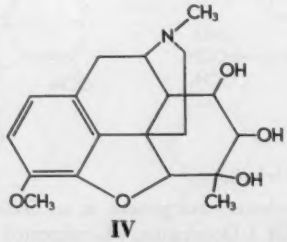

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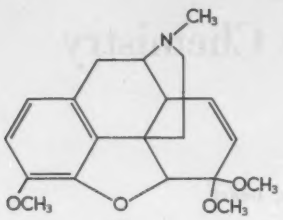

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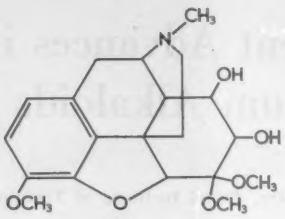

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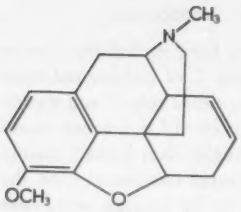
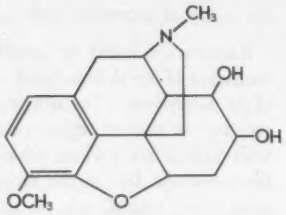
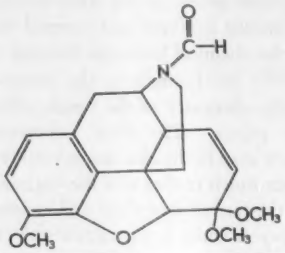


VII



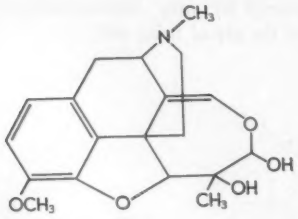
VIII



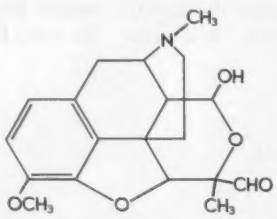
IX

It is interesting to note that in the case of codeinone dimethyl ketal (V) a competitive reaction also took place — namely, oxidation by osmium tetroxide alpha to the nitrogen atom, affording *N*-formyl-*nor*codeinone dimethyl ketal (IX).

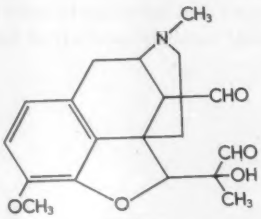
The glycols prepared were then further oxidized in order to cleave ring C. For example, upon oxidation in acid solution, IV consumed one mole of periodate, yielding various compounds formulated as X and XI (or XII).



X

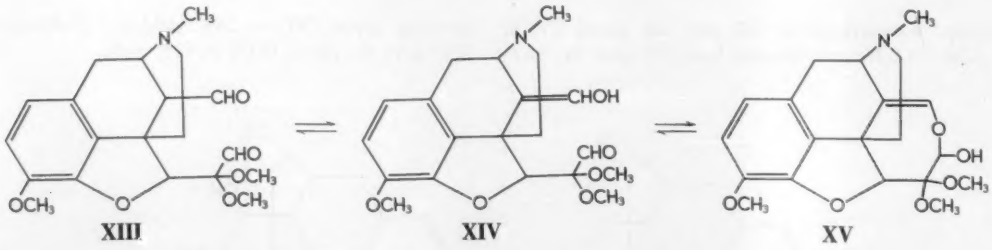


XI



XII

The hemiacetal formulations (X and XI) received further support from the products obtained by periodate oxidation of VI. Here again various products were obtained according to pH, and these were formulated as XIII, XIV and XV, which may be easily interconverted.

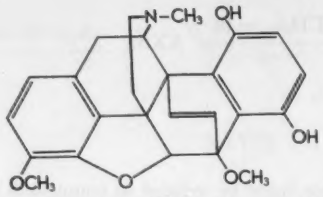


XIII ⇌ XIV ⇌ XV

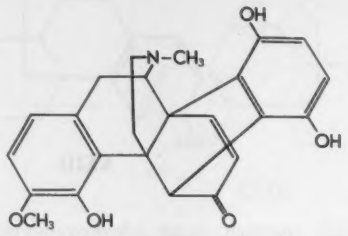
II. *The Structure of Flavothebaone*

Early in 1953 the reviewer was present at an Oxford Alembic Club lecture by Dr. J. Dominguez, who presented an account of work he had carried out on a reaction which at that time was very difficult to interpret. We now have before us an exhaustive research embodied in a series of four recent papers

(3-6) which are the culmination of beautifully executed experimental work and brilliant deductive reasoning by Bentley and his co-workers. A very complex problem appears to have been solved, and convincing evidence and reasoning allow us to accept with confidence the following structure (XVII) for flavothebaone. The stereochemistry and mechanism for the rearrangement of thebainequinol (XVI) into flavothebaone are reasonably explained (4).

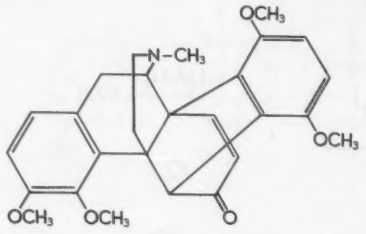


XVI

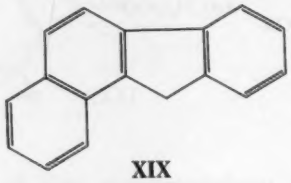


XVII

The complex series of transformations involved in the exhaustive methylation of flavothebaone trimethyl ether (XVIII) culminating with derivatives of the chrysofluorene ring system (XIX) has also been elucidated (3).



XVIII



XIX

Fitting into the structural scheme in accordance with the above formulation for flavothebaone (XVII), various other flavothebaone derivatives have been degraded — e.g., to thebenone type compounds (5) and simpler derivatives, again believed to be based on the chrysofluorene skeleton (6).

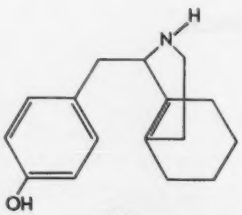
For the details of these investigations the reader is referred to the original papers. It is hoped that further interesting communications will soon be forthcoming from Dr. Bentley's Aberdeen laboratories, embodying the structural elucidation of other Diels-Alder adducts of thebaine.

III. *Synthetic Morphinans*

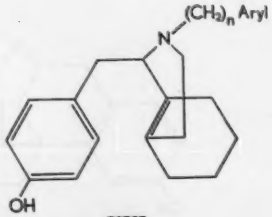
The Hoffman-La Roche laboratories at Basel have continued their synthesis of morphinan derivatives and have reported the preparation of several compounds characterized by extremely intense analgesic activity (7).

Several synthetic approaches were used. The starting materials were either (—)- and (+)-1-(*p*-hydroxybenzyl)-octahydroisoquinoline (XX) or (—)- and (+)-3-hydroxy-morphinan (XXIII).

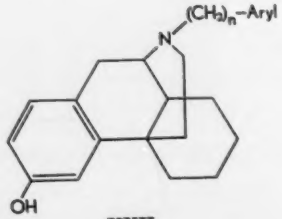
1-*p*-hydroxybenzyl-1,2,3,4,5,6,7,8-octahydroisoquinoline (XX) was alkylated at the nitrogen atom and the *N*-alkyl derivative (XXI) was cyclized to the *N*-substituted morphinan (XXII).



XX

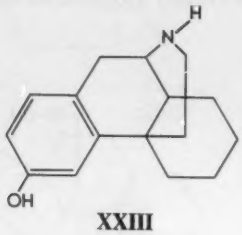


XXI



XXII

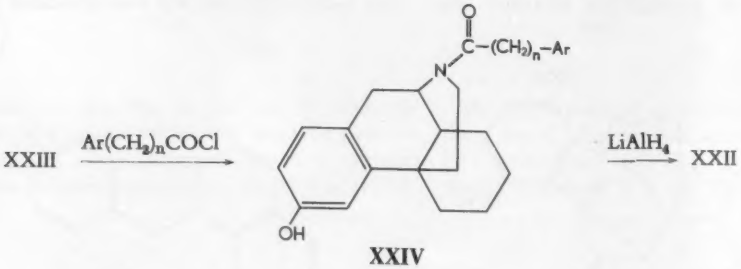
Alternatively, 3-hydroxymorphinan (XXIII) already containing the tetracyclic portion of the opium alkaloid skeleton was treated with arylalkyl bromides again yielding compounds of type XXII.



$$\text{Aryl} - (CH_2)_n - Br \longrightarrow \text{XXII}$$

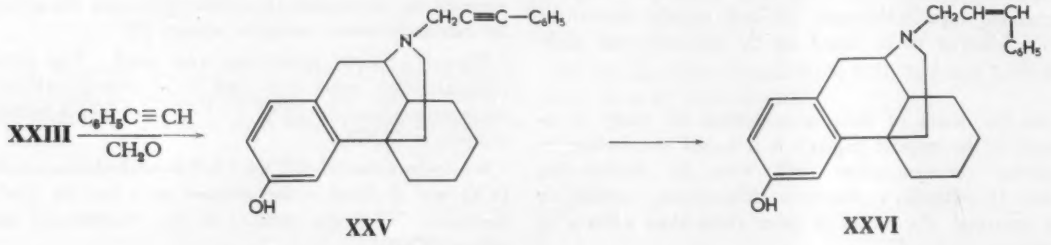
XXIII

Another synthetic approach, using 3-hydroxymorphinan as the starting material, was treatment with arylalkyl acid chlorides. *N*-acyl-morphinans (XXIV) were thus obtained and these could be reduced to compounds of type XXII by reduction with lithium aluminium hydride.

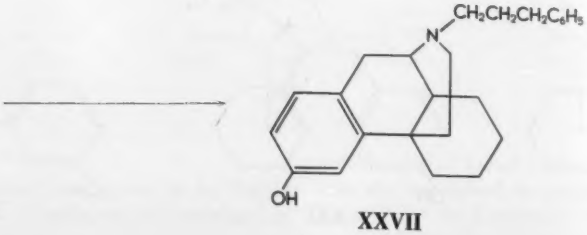


XXIV

Other types of arylalkylmorphinans could be obtained by two additional routes. Treatment of (—)-3-hydroxymorphinan with phenylaceteylene and formaldehyde affords (—)-3-hydroxy-*N*-phenylpropargyl-morphinan (XXV). Partial hydrogenation of the triple bond affords the *N*-phenylallyl derivative (XXVI) whilst its full hydrogenation again affords a compound of type XXII, namely the *N*-phenylpropyl derivative (XXVII).

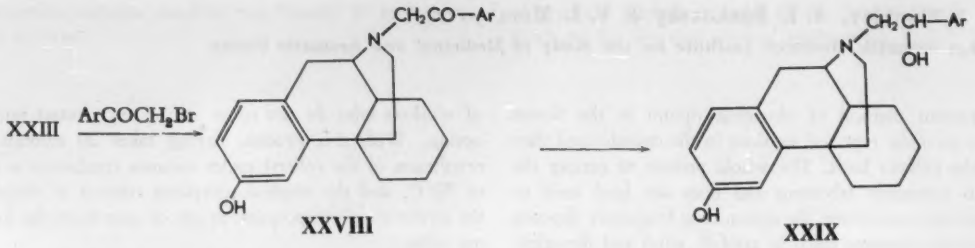


XXV **XXVI**

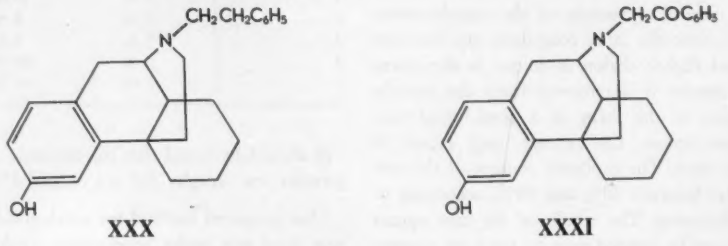


XXVII

Treatment of 3-hydroxymorphinan with bromo-acetophenone or its homologs gives *N*-phenacyl derivatives (XXVIII) and these can be reduced to the *N*-acyl-hydroxyalkyl compound (XXIX).



(—)-3-Hydroxy-*N*-phenylethyl-morphinan (XXX) and (—)-3-hydroxy-*N*-phenacyl-morphinan (XXXI) and several of their derivatives showed 50-70 times the analgesic activity in animals as compared to morphine itself and are several times more effective than (—)-3-hydroxy-*N*-methyl-morphinan (Dromoran).



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Mechanical drying of raw opium

By V. A Shevelev, A. I. Bankovsky & V. I. Muravyova,
All-Union Scientific Research Institute for the Study of Medicinal and Aromatic Plants

The present method of obtaining opium in the Soviet Union is to make repeated incisions in the capsules and then collect the effluent latex. The whole process of getting the opium is extremely laborious and does not lend itself to mechanization; moreover, the opium crop frequently depends on fortuitous elements (such as rainfall, wind and drought).

The capsules are cut and the opium is collected at the particular phase of the plant's growth known as the stage of technical maturity, which coincides with the lactic maturity of the seeds. The capsules are incised during the latter half of the day with a specially designed three-bladed knife, and the effluent latex is allowed to remain on the capsules overnight, during which time the latex coagulates and becomes somewhat thicker and slightly darker in colour. In the morning, usually before sunrise, it is removed from the capsules with a special scraper, in the form of a semi-liquid substance known as raw opium. On average, each capsule is incised three or four times. The moisture content of the raw opium collected varies between 40% and 60%, according to the conditions of cultivation. The whole of the raw opium collected each day must be handed over to the state organization concerned.

The raw opium thus obtained in the Soviet Union is used exclusively for medical purposes.

To obtain opium in powder form, the former practice was to spread the raw opium thinly several times a day on sheets of parchment paper and dry it in the sun for six to eight days. The dark brown viscous mass of opium was then cut up into briquettes. These were dried in a drying kiln for ten to twelve days to 8% moisture, and then ground into powder.

This method of drying inevitably involved some loss of morphine and other alkaloids, and also meant employing a large number of workers, who were in contact with the raw opium for long periods during the drying process.

Experiments which we made showed that the process of drying the raw opium on parchment paper resulted in a morphine loss of up to 8%, owing to the action of the atmospheric oxygen and direct sunlight, while the subsequent drying of the briquettes in the kiln resulted in a further loss of up to 5%, making a total loss of up to 13% of the morphine content of the opium.

With a view to improving the conditions of work of those engaged in producing opium powder and eliminating losses of morphine and other alkaloids during drying, experiments were made to evolve a more efficient drying method.

It was found that raw opium can be successfully dried in a vacuum roller machine in which all the processes are fully mechanized, and which can be serviced by a mere handful of workers who do not come into direct contact with the opium. With this process, drying takes 20 seconds (one revolution of the rollers) under vacuum conditions at 60° C to 70° C, and the original morphine content is retained in the resulting opium powder, as can be seen from the following table :

Raw opium, sample number	Morphine content, in % of absolute dry weight		Moisture content of opium powder, %
	in raw opium	in opium powder	
1	9.55	10.03	2.29
2	8.80	8.80	3.20
3	9.66	9.89	2.60
4	9.66	10.01	3.40
5	11.95	11.98	0.46

It should be noted that the moisture content of the opium powder test samples did not exceed 4%.

Our proposed method for mechanically drying raw opium was tried out under production conditions with a Sangerhausen-type vacuum roller dryer.

Results of mechanical drying of five tons of raw opium

Lot number	Raw opium processed			Opium powder yield		
	Raw opium in kg	Morphine content of raw opium, in %	Morphine content, in g	Opium powder in kg	Morphine content, in % of weight (air dried)	Morphine content, in g
1	1012.140	5.850	58758.282	495.33	11.95	59209.396
2	846.050	5.460	46172.000	375.20	11.66	43767.800
3	713.080	5.240	37414.142	342.80	11.11	38079.660
4	895.294	7.197	64434.786	503.15	13.09	65905.075
5	878.030	5.670	49793.028	429.97	11.40	49009.556
6	812.645	6.200	50379.756	443.04	11.12	49267.820
TOTAL	5157.239		306951.99	2589.49		305239.3

The morphine retention rate for the mechanical drying of 5 tons of raw opium, according to the gramme figures, was 99.43%.

Proceeding from these laboratory and production-scale tests, the conditions recommended for mechanically drying raw opium are as follows : pressure of steam for heating the rollers, 0.5-1.0 at ; pressure of steam for heating the body of the machine, 3-4 at; vacuum in the chamber, 0.7-0.75 at; temperature in the chamber, 60-70°C. The raw opium is pumped

into an automatic measurer, from which it is gravity-fed in portions on to the rollers. The automatic measurer cylinder has three cavities, and is geared to the rollers as it turns. Drying takes 20 seconds — i.e., one revolution of the rollers. A two-roller vacuum machine can handle 30 kg. of raw opium an hour.

The morphine retention rate amounted to 99.43% with mechanical drying (in the processing of 5 tons of raw opium), whereas the old method of sun-drying and kiln-drying gave an 87% morphine yield and also required a large number of workers. Opium powder in the Soviet Union is now produced by the new method exclusively.

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Experiments which we made showed that the process of drying the raw opium on parchment paper resulted in a morphine loss of up to 8%, owing to the action of the atmospheric oxygen and direct sunlight, while the subsequent drying of the briquettes in the kiln resulted in a further loss of up to 5%, making a total loss of up to 13% of the morphine content of the opium.

With a view to improving the conditions of work of those engaged in producing opium powder and eliminating losses of morphine and other alkaloids during drying, experiments were made to evolve a more efficient drying method.

It was found that raw opium can be successfully dried in a vacuum roller machine in which all the processes are fully mechanized, and which can be serviced by a mere handful of workers who do not come into direct contact with the opium. With this process, drying takes 20 seconds (one revolution of the rollers) under vacuum conditions at 60° C to 70° C, and the original morphine content is retained in the resulting opium powder, as can be seen from the following table :

Raw opium, sample number	Morphine content, in % of absolute dry weight		Moisture content of opium powder, %
	in raw opium	in opium powder	
1	9.55	10.03	2.29
2	8.80	8.80	3.20
3	9.66	9.89	2.60
4	9.66	10.01	3.40
5	11.95	11.98	0.46

It should be noted that the moisture content of the opium powder test samples did not exceed 4%.

Our proposed method for mechanically drying raw opium was tried out under production conditions with a Sangerhausen-type vacuum roller dryer.

Results of mechanical drying of five tons of raw opium

Lot number	Raw opium processed			Opium powder yield		
	Raw opium in kg	Morphine content of raw opium, in %	Morphine content, in g	Opium powder in kg	Morphine content, in % of weight (air dried)	Morphine content, in g
1	1012.140	5.850	58758.282	495.33	11.95	59209.396
2	846.050	5.460	46172.000	375.20	11.66	43767.800
3	713.080	5.240	37414.142	342.80	11.11	38079.660
4	895.294	7.197	64434.786	503.15	13.09	65905.075
5	878.030	5.670	49793.028	429.97	11.40	49009.556
6	812.645	6.200	50379.756	443.04	11.12	49267.820
TOTAL	5157.239		306951.99	2589.49		305239.3

The morphine retention rate for the mechanical drying of 5 tons of raw opium, according to the gramme figures, was 99.43%.

Proceeding from these laboratory and production-scale tests, the conditions recommended for mechanically drying raw opium are as follows : pressure of steam for heating the rollers, 0.5-1.0 at ; pressure of steam for heating the body of the machine, 3-4 at; vacuum in the chamber, 0.7-0.75 at; temperature in the chamber, 60-70°C. The raw opium is pumped

into an automatic measurer, from which it is gravity-fed in portions on to the rollers. The automatic measurer cylinder has three cavities, and is geared to the rollers as it turns. Drying takes 20 seconds — i.e., one revolution of the rollers. A two-roller vacuum machine can handle 30 kg. of raw opium an hour.

The morphine retention rate amounted to 99.43% with mechanical drying (in the processing of 5 tons of raw opium), whereas the old method of sun-drying and kiln-drying gave an 87% morphine yield and also required a large number of workers. Opium powder in the Soviet Union is now produced by the new method exclusively.

The battle against opium in Iran — a record of progress

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On 7 October 1955 the Majlis passed the new Opium Law, sponsored by Dr. J. S. Saleh, M.D., the Minister for Health in the Government of Iran. In the *Bulletin on Narcotics* (Vol. VIII, No. 3, July-September 1956) an article appeared from the pen of Dr. Saleh, which gave the text of the new law, together with a dramatic exposé of the circumstances under which the law was passed. The law was drastic : it prohibited the cultivation of the poppy and the use, import, movement and export of opium and opium products. It indicated which ministries of the Government of Iran were competent to administer it, and it made arrangements for the implementing of its provisions within a fixed limit of time.

It is the purpose of this article to tell the story of the battle against opium which was joined in Iran with the passing of the law of 7 October 1957; to estimate progress[k]; and to tell, as far as may be possible without straining at prophecy, what may be the future of this effort. The effort in itself is wholly commendable. Iran found a moral courage and a vigour which deserve the highest praise, in determining to eradicate the traffic in opium. It is fair to say at the outset that this effort was not a flash in the pan. In spite of difficulties caused by insufficient organization, material and funds, the battle has been remarkably successful in the two years which are now under review. There is no reason to despair of the future.

Regulations under the new law were passed giving in detail the means by which it was to be implemented. These regulations covered in a comprehensive form the ban on cultivation of the opium poppy ; the ban on the use of cafés or hotels for drug taking ; the prohibition on the preparation or import of material for smoking opium ; the treatment of addicts ; a general prohibition on the use of narcotics, with penalties ; arrangements for technical assistance, advances and loans to aid farmers who had been hard hit by the ban on poppy cultivation ; the duties of the various officials ; and, finally, the creation of an organization which would oversee the work of implementing the law. This organization, the full title of which is translated shortly as " The Independent Organization for the Control of Opium " derives from the old Opium Monopoly Department, the main function of which, the taking over of opium from the cultivator for government use, has now disappeared. The stocks of opium which were held by the Government of Iran when the new law was passed were to be the concern of the Ministry of Finance ; they are now being dealt with by a new ministry, that of Customs and Monopoly. Those officers and men who were not needed for the Department of the Liquidation of Stocks formed the new Department, the function of which is the combat against the drug. The control of this new department vests in a committee of five — a former Minister for Agriculture as chairman, two doctors, a judge and a senior officer of the Ministry of Finance.

All the members of the committee are eminent in public life in Iran, or in their own professions. The constitution of the committee also points a moral on the view taken in this country of the opium traffic. The emphasis is on the sociological aspects of the traffic : public health ; agriculture and the need for an alternative source of income ; economics and the effect of the loss of the trade in opium on finance and economics, rather than on the criminal ramifications of the narcotics traffic. It is, in fact, important to remember that in underdeveloped countries, poverty and lack of health facilities, combined with the traditional use of opium for quasi-medical purposes, introduce a factor into consideration of a narcotics problem which is in fundamental distinction from the view taken in some other countries. Not vice or crime, but poverty and sickness, are the main objectives of action. The controlling body is therefore a multi-purpose body, which was designed to cover as completely as possible the whole field of action. The organization which works directly under this body has two functions. There is a central office in Tehran, which acts as a general secretariat to the controlling body. There are offices in ten prominent centres — Quum, Isfahan, Shiraz, Hamadan, Malayer, Kermanshah, Tabriz, Resht, Shahi and Meshed — which are designed to be centres of preventive activity in the areas where the poppy was most frequently cultivated in the past, or where addiction was most frequently found. In addition, there is a branch in the central office in Tehran which functions both as an intelligence centre and as a headquarters for preventive activity. The outstation offices, combined with the central office in Tehran, form a strategic network covering the nerve centres of illicit production and distribution, in addition to providing the organizations with administrative control. In this part of the organization, a staff of 577 is employed. In addition, there are 397 officers and men posted to smaller stations which are situated almost entirely on routes by which it is known that contraband may be carried. There are fifty-three of these stations, which now operate under the control of the Finance Agency of the ostan (district) in which they are placed. Finally, there is an Opium Branch in the Ministry of Health which ensures liaison with the controlling ministry.

The Government of Iran realized when the law was passed that they had a very heavy task on their hands, and that while the immediate impact of the law might be salutary

— as indeed it was — a serious administrative effort would be needed in order that pressure, once applied, might be maintained. Greater experience was needed in the organization of such battles as had now been joined; more material had to be found, and funds were needed which were not available in the country. An application was therefore made to the United Nations for assistance : technical, financial and in respect of material. The assistance which was asked for was designed to cover the whole field in which the new law would operate : agriculture and help to the farmer; public health and the rehabilitation of addicts; propaganda and enforcement. It is the standard practice of the United Nations to give expert advice and to train the nationals of the country which asks for assistance, to enable them to continue to operate after receiving that advice. Funds and material in any considerable quantity are not usually available. The United Nations therefore arranged for advisers to be appointed in three fields : administration, agriculture and medicine; at the same time, a number of fellowships were offered to Iranian nationals for training in the special fields which were now opened up, such as the laboratory techniques for the recognition of types of opium. An adviser has also been appointed by the United States Overseas Missions, who has expert knowledge of narcotics enforcement administration. Limited material and funds have been made available by the United Nations, which are to be used in the field of propaganda and education.

In two years, there is a substantial record of achievement under the new law, and also no failure to recognize that there are difficulties which have not yet been solved, and that much remains to be done if the battle is to be sustained. It is evident that the most important single factor is the interdiction of cultivation. This has been remarkably successful, even in the present season, the third since the new law was passed. Personal observation, reports and statistics bear out the conclusion that there is little poppy cultivation, except in distant tracts in mountain valleys which are not easily accessible to the forces of government. Cultivation has been reduced from an estimated 20,000 hectares to practically nil. That this result owes a good deal to preventive action is shown by the figures of cultivation dealt with under the new law. Six thousand, eight hundred and twenty-one tracts were destroyed (the poppy cultivation was ploughed in), amounting in all to 581.43 hectares of land.

It is necessary to remember that in October 1955 there were stocks of illicit opium in the hands of traffickers. It is not known, for obvious reasons, what was the extent of these stocks. They have been estimated as being enough even for six years' use in the illicit market. It is sufficient to recognize that such stocks did exist, and that they are finding their way into the illicit market now. Pressure is being maintained on traffickers. But the price that can now be obtained — twenty or thirty times the price at which the Government of Iran is now selling for export from its stocks — is such that the financier and organizer of the traffic can still be sure of a substantial profit. In order that he may maintain his profit, there are signs that dilution is being used to a significant degree. A recent large seizure of stick opium, made up to imitate the form in which opium was sold for local consumption by the Government before the passing of the new law, was estimated by experts of the department to contain not more than 10% of opium — 90% was adulteration. A mixture of dross with fresh opium is popular with addicts. It is stated that this mixture has more deleterious effects than pure opium. Seizures of opium and opium products in the last year amounted to over 1000 kg. In the last complete year before the passing of the new law, the weight of opium and opium products seized was a good deal more than this : it is fair to conclude that there is less opium in the illicit market than there was, but that pressure is needed to an acute degree. Enforcement of the law needs to be improved. Above all, investigation needs to be carried to a higher level, on which it may be possible to take action not against the carrier or the immediate user of a small quantity of opium, but against the financier and organizer who is responsible for the maintenance of the illicit traffic, with all its consequences on the health and the economy of the country.

It is good to know that the amount of Iranian opium that has found its way into the illicit market outside the country has been greatly reduced. Its place is being taken by opium which derives from other sources. The demand on the world illicit market remains, and the problem of stopping supply and checking illicit use is as much a problem in the international field as it has been in Iran; indeed, as it still is in Iran.

The interdiction ot cultivation in Iran and success against illicit use of the drug are of little use unless supply from outside the country is also stopped. The fact is that the creation of a partial vacuum in supply, which has been filled in part by local traffickers, as has already been described, has given an opportunity to smugglers who deal in the produce of neighbouring countries. The problem is the more serious since much of the frontier of Iran consists of a difficult mountain and desert terrain the patrolling and guarding of which present many problems. The stand which has been taken by Iran in respect of its own supply contains a lesson for all producing countries.

The stocks held by the Monopoly Ministry of the Government of Iran represent a supply which will last for many years for medical and scientific purposes. They are held under strict control, and pass into consumption from time to time either on a requisition from the Ministry of Health — for internal consumption through Government hospitals — or by sale to a foreign government if there is a demand from abroad. The intention of the new law was that addicts should report themselves within six months. Government servants were to be examined, in order to see whether they had been habitual users of the drug, since addiction in a government servant was a sufficient ground for dismissal. Many government servants have been examined, and many members of the public have been treated both in government and private hospitals. But the position is far from satisfactory and far from clear. It is now held by the Ministry of Health that the figure of addicts given by Dr. Saleh at the time at which the new law was passed — 1,500,000 addicts

out of a total population of about 19,000,000 — is perhaps an understatement. The figure may be as high as 2,000,000. It is true that the number of people who are found using the drug is still considerable, and it is true also that the number of people who have been treated at their own wish in government hospitals is far from insignificant — 40,000 in two years. Nevertheless, until there is a fairly firm statistical basis for proceeding to conclusions, the position in regard to addiction must be held to be obscure. It is certain that addiction was and still is a most serious problem. Its real extent can be discovered by the collection of accurate figures. For this purpose, as a beginning, the use of a form of report to be submitted by all authorities, hospitals, police, etc., who may have to do with addicts, has been proposed. A second step, when more information is available, may be to distinguish between addicts and users who are not strictly addicted to the drug. It has been stated again that a census of addicts is contemplated in one or two other countries having a similar problem. It may be that such a census could be attempted in Iran. Even if it were only partly successful, its results would go a long way towards throwing the light of factual information on a subject where information has so far been largely conjectural. This is not to minimize the known seriousness of the problem. It is a recognition of the fact that more statistical information is essential, in order that a full frontal attack on the problem may be organized.

It will be seen that the problems which have been raised by Iran's bold attempt to eradicate the opium evil are many and grave. The first step which was regarded as essential in order to deal with them was a review of the opium administration. The request for assistance which was made to the United Nations was in part for the appointment of an administrative adviser ; in addition, as has been indicated, the services of an experienced narcotics police administrator have been secured from the United States Overseas Mission. The review of the narcotics organization which has been carried out has been thorough. It has covered basic organization ; control ; preventive work ; inspection ; training ; pay and conditions of service ; rewards ; mobility ; and the need for an improved investigation branch. No final conclusion has yet emerged from this review : whatever the conclusion may be, there is no doubt that it will be the result of a survey which has lacked nothing both in thoroughness and in good will. A more effective administration is bound to emerge. In addition, a statistical scheme has been suggested which, it is hoped, will improve both the statistical bases on which conclusions are founded in respect of work and organization in the country and statistical reporting to the United Nations. A renewed propaganda drive against opium has been suggested, which will use the radio and press, and will include the writing and printing of pamphlets for the public schools and colleges. A proposal to make use of the film as a medium of propaganda is also under consideration.

A study of agricultural problems is under way, in the hands of experts of the Food and Agriculture Organization, and it is expected that study of certain aspects of the many health problems which arise from the use and abuse of the drug will soon begin.

A detailed review of the frontier problem has been suggested, based on a plan for frontier control which, it is hoped, will not prove to be either too expensive or too complicated for use after it has been adapted to local conditions. It is generally recognized that an effective frontier system is a *sine qua non* of an effective administration.

Consideration of the various problems which have been outlined leads back inevitably to the questions of money and material which were raised at an early stage of action under the new law by the Government of Iran. Where money has been made available by the Government of Iran, as in the case of aid to farmers, proposals for its utilization have been suggested. But a basic difficulty in the whole treatment of the opium problem in Iran is financial, in the wider sphere. To modernize and expand the enforcement administration will be expensive ; to improve the health administration, when the basic data to which allusion has been made are available, will be even more expensive. Here, too, there is the difficulty that doctors are not made in a moment, and that this is a specialized field of medicine : public health in the wider sense does need attention ; but the cure and treatment of narcotics addicts is only a part of this huge field. The position at present is that investigation has been almost completed and data are being assembled : the stage of planning has been reached. At this stage, it is essential to see what resources can be made available locally. If those resources are not adequate, the problem comes into the international field. The Government of Iran has spared no effort to realize its problems; it will make the utmost use of local resources, but it may be necessary to place the problem open to international consideration if these resources are insufficient.

One word dominates the whole picture : poverty. Drug addiction does not arise in a limited criminal class in connexion with criminal activities. It is found anywhere in the nation — among farm workers, factory workers, truck drivers, labourers, restaurant employees. It may arise from sickness or pain, or simply from disgust with life. Addiction is found in most age groups ; but exists particularly amongst able-bodied workers of all types. A low standard of living, and working conditions which need much reform, combine with ill-health to create a climate in which opium seems like the gift of the gods to ill-used humanity. This is not a condition which is peculiar to Iran. It is found in most underdeveloped countries. It is significant that in such countries in the Middle East and the East there is usually a narcotics problem. It is not merely the poverty of the great mass of the people which dominates the problem, although this poverty is a basic cause. It is also the poverty of resources of the country. A modern administration needs trained manpower and expensive equipment. The effectiveness of the work of any administration is limited by the standards of working and of training of its personnel, and by the manner in which they are equipped for the special tasks for which they are employed. Even in developed countries, the fight to obtain the manpower and the machine-power that is needed for the many tasks which now devolve upon a government is far from easy. It is the more difficult in a country

which has far more limited resources; on which from the very nature of its position there is a far more extensive set of demands.

A great effort has been made in Iran; the stage is set for a determined continuance of the effort. The future will depend on three factors. First, the long-term provision of expert aid, until a stage has been reached at which planning is completed and the training of the local officers has come to the point at which they can take over the whole task; second, the training of Iranian officers both abroad and in Iran, in numbers and to a stage of efficiency which will enable them to undertake the work; and third, the provision of such equipment as mature consideration indicates to be essential by aid, where the Iranian Government is unable to make the necessary provision from its own resources. This issue will inevitably be raised again. Indeed, it must come up at various stages in the working out of the continued battle against opium, as needs are found; as smugglers think out fresh means of working which need fresh counters from the side of the Government; and as greater knowledge accrues in the spheres of public health and agriculture. The way cannot be easy, and there is no promise of success either soon or finally. The struggle will go on. It is a matter for deep satisfaction that the battle was engaged, and that it has been so well maintained up to the present time. It is not merely in the interest of Iran that it should be equally well maintained in the future, but in that of the whole world.

The cocaine problem in India

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I. Introduction

The use of coca leaf for euphoric purposes was started centuries ago by the natives of certain parts of South America. Its various aspects and the attitude of the governments involved and of the international community have been dealt with in several articles published in the *Bulletin on Narcotics*.*

The active principle of the coca leaves, the alkaloid cocaine, was discovered in 1859–60, but it was only after 1884 that the importance of the plant from the medicinal point of view extended rapidly. Export of dry leaves from South America started from that time. About 1890, factories were opened in Peru to extract cocaine in crude form for export with a view to saving the cost of transport of the whole leaf. It was in this way that the alkaloid replaced the leaves, and knowledge of the effect produced by it spread to other parts of the world. In 1890, 1,730 kg of crude cocaine were exported, increasing to 10,600 kg by 1901. Between 1890 and 1910, cocaine began to be fairly largely used in the United States of America for euphoric purposes. Negroes particularly used this drug in the form of snuff, and cases of ulceration of the septum of the nose were not infrequently seen among them.

The knowledge of the remarkable effect produced by cocaine gradually spread to Europe, India and China. It was thought at that time that administration of cocaine in cases of opium and morphine addiction and in alcoholism helped to break these habits. Unfortunately, instead of curing morphinism it produced morphino-cocainism. During the First World War, there was so much increase of habitual use of cocaine in Europe that vigorous measures were taken by the authorities to put an end to this practice.

The successful use of cocaine for producing local anaesthesia began to be increasingly appreciated in the early parts of the twentieth century, and it was considered worthwhile to produce it by synthesis. Extraction from the leaf, however, was easier and cheaper and plantations were started in Java and elsewhere. The leaf from Java was sent to factories in Europe, America and Japan for processing, and the South American product was practically driven from the market. In 1922, 1¼ million kg of leaves were exported from Java with a cocaine content of 1.5%.

Species Erythroxylum in India. Erythroxylum coca is not indigenous to India. No reference is to be found in the ancient Sanskrit literature about this shrub or the use of its leaves or the properties possessed by them. The only references in medical literature that exist are of very recent origin, and concern the use of the alkaloid cocaine, and not the leaf itself. The variety *Erythroxylon monogynum* is said to be indigenous to India (Madras), but it does not contain cocaine or any of the related alkaloids. This variety has smaller leaves than *E. coca* and can stand higher temperatures; and it is thought that if cultivated under proper conditions it might produce cocaine. Two other varieties of *Erythroxylon* are believed to grow indigenously in Bombay

* See especially Vol. I; Vol. II, No. 1; Vol. II, No. 4; Vol. IV, No. 2; Vol. IV, No. 3; Vol. IV, No. 4; Vol. V, No. 4.

State, but if they grow at all they must be extremely rare. One of them yields a mere trace of cocaine, the other does not yield any alkaloid at all. The habit of chewing coca leaves consequently never existed in India.

In 1870 *E. coca* was brought to Ceylon from the botanical gardens at Kew, London, and in 1883 it was brought over to India. When carefully cultivated under suitable conditions, the leaves have been found to be rich in cocaine, the yield increasing with the age of the plant. In India, it was observed that the best results were obtained from plants grown on the uplands of the Nilgiri hills; those planted in the hot low plains did not thrive, and eventually died out.

E. coca has never been cultivated in this country on a large scale. Some time ago (1926) an account of the prevalence of the habitual use of cocaine appeared in the English daily press in India. It was suggested that cocaine bearing *Erythoxylon coca* was growing wild all over the country, that people were learning the habit of chewing the coca leaf, and that there might be secret factories for the manufacture of cocaine. It was argued that large quantities of the drug coming from an unknown source were seized on railways, and that the cocaine habit was spreading rapidly. The alleged cultivation of the coca plant was also referred to at a meeting of the Advisory Committee of the League of Nations on Traffic in Opium and other Dangerous Drugs in 1925. Careful inquiries were made by the Government of India, and it was established that neither *Erythroxylon coca* nor any other plant from which cocaine could be produced was culativated in India. *E. coca*, far from growing wild all over the country, is not known to grow in a state of nature anywhere in India. A few plants were found in some of the Nilgiris estates, which were in all probability relics of the experiment made in 1885, but even these contained little or no cocaine. The manufacture of cocaine is a highly technical process, and there is no ground whatever for the belief that cocaine was ever secretly manufactured in India.

II. Habitual Use of Cocaine in India

Early References

Near the end of the nineteenth century, it was realized that cocaine was being used in certain parts of the States of Bengal and Bihar for its euphoric effects. The earliest record of its use came from a small town named Bhagalpur in Bihar State. The story is related of a rich land-owner who contracted the habit accidentally after using cocaine to relieve dental pain. So extraordinary were the effects produced that not only did he become habituated to its use, but he passed on the habit to many others. In course of time, it was observed that cocaine was being secretly sold by certain agencies to people who were taking it in prepared betel leaf (pan). A class of pedlars had sprung up who were selling the drug not only to grown-up people but also to teen-age schoolboys. It was usually sold in packets or "lifafas" (envelopes) of a half grain each.

In this way the habit spread to large towns such as Calcutta and others. The habit appears to have spread along two main rail routes to northern India. It worked its way up to towns like Benares, Lucknow, Rampur, Saharanpur and Ambala on the one side, and through Allahabad, Kanpur, Agra, Muthra and Delhi on the other. We were informed that in Delhi the habit existed on a fairly large scale in the early part of this century. There, it is said to have spread through the agency of a medical practitioner who prescribed it in large quantities as a stimulant and as a tonic. Trained midwives are said to have been responsible for its introduction among the womenfolk of certain towns. Shawl merchants and dried-fruit traders from the north, who were in constant communication with Calcutta, took the drug to Amritsar, Lahore and Peshawar. An excise officer of the North-West Frontier Province (now in Pakistan) said that people from Peshawar were in a great measure responsible for the traffic in cocaine in the country. Large quantities of "charas" (resin of *Cannabis sativa* manufactured in central Asia) were smuggled through the frontier area at a low price. This was carried by them to big centres such as Bombay and Calcutta, where it was sold at high profit to traffickers. The proceeds of these sales were utilized to smuggle cocaine back from the seaport towns to different large towns of the country.

Control over the Import and Sale of Cocaine

When the habitual use of cocaine began at the end of the nineteenth century and the beginning of the twentieth century, restrictions on the import, sale and use of this drug were not strictly enforced. The excise authorities soon realized the seriousness of the situation, and regulations were brought into force to ensure strict control of the import and sale of cocaine. The sale of the alkaloid to the general public was forbidden, and even the sale by licensed druggists and chemists to medical practitioners and dentists was strictly controlled. No one was allowed to possess coca leaf, alkaloids of coca, or any preparations made from them, or preparations containing ecgonin or any substance chemically allied to cocaine or having similar physiological effects, except under a special licence. The possession of these drugs under licence was also strictly controlled. In spite of this, Chuni Lal Bose, Chemical Examiner to the Bengal Government, writing in the *British Medical Journal*, 1913, said, "Despite the vigilance of the excise authorities and notwithstanding the stringent measures adopted by the Government against the possession and sale of this substance by unlicensed persons, there is reason to believe that the cocaine habit has much increased and is rapidly spreading."

The excise authorities, of course, had knowledge of the individuals who were responsible for the cocaine traffic in various parts of the country. In fact, lists of such persons had been prepared and circulated. They were, however, powerless to put an end to their activities because of the great difficulty of proving the offence in courts of law. Besides, many of the persons dealing in this traffic were dangerous individuals, and people were afraid to come forward and give evidence against them. More often than not the cases against them failed.

Extent of the Habit during the Period between the Two World Wars

It is not possible to say with any degree of accuracy to what extent the habitual use of cocaine existed in India at that time. Luke (1914) said that the habit of taking cocaine was by no means confined to the poor and uneducated classes. Information gathered from investigations in various states of India showed that at first only members of the medical profession knew about the euphoric properties of cocaine, and that it was from them that the lay people in towns learnt about its stimulating and pleasure-giving properties. At the outset, when the restrictions regarding the possession and sale of cocaine were not strict, the habit quickly spread from one town to another on account of the transport facilities afforded by railways, which were developing in the country at that time. The stimulant effects produced by the drug were a great attraction to the type of individual who was ignorant of the evil effects it produced on the body. Moreover, the enormous financial gain which the dealers in this nefarious traffic obtained soon induced them to employ agents to push on their trade by advocating and popularizing the use of the drug. It thus came about, that even when restrictions were imposed, the use of this drug was not significantly curtailed for some time. On the contrary, it increased, and cocaine became a well-known commodity to many of the inhabitants of large towns in India.

It was popularly believed to be a sexual stimulant, and many started taking in to increase their virility. The other attraction for its use was that it had a most extraordinary, though temporary, effect in rapidly overcoming physical fatigue and mental depression. For these reasons, its use rapidly spread among the upper and educated sections of society in towns. The drug was smuggled into Bombay from abroad, and its use spread from one town to another in the State of Bombay and to other states. The remarkable fact was that although the large towns along the main railway lines were affected, those along the branch lines generally remained untouched. The only part of India in which the habit did not spread to any great extent was south India, particularly Madras State.

It was very difficult to form any accurate estimate of the incidence of the cocaine habit in different parts of the country because the habit was considered to be so disgraceful that no self-respecting individual would own up to it. Besides this, the sale as well as the possession of cocaine had been declared illegal, and the possessor of the drug as well as the dealers were liable to prosecution and punishment under the Dangerous Drugs Act. Inquiries were therefore very difficult and delicate and sometimes even dangerous. Only after several years of patient investigations could some idea be formed of the incidence of the habitual use of cocaine among the people in different states. In this work the collaboration and help of the excise authorities were invaluable. It was surprising to find that the habit was spreading among the educated classes and well-to-do people in towns. The lower strata of society were also taking the drug. Even women of high-class families were taking the drug, particularly in Uttar Pradesh State. The drug was invariably taken in betel leaf, which they were in the habit of chewing all day long. The dealers in this drug fully realised that unless they got hold of wealthy families who could afford to pay a high price it would not be worth their while to carry on this nefarious and rather hazardous trade. They therefore tried to introduce the drug into the homes of rich people, chiefly through the agency of betel sellers and servants.

As the popular way of taking the drug in this country was and still is to add it to betel leaf, it was quite an easy matter for a designing person to put the drug in a " pan " (prepared betel leaf) and introduce it into the household of unsuspecting individuals. The immediate effects of the drug were so striking and the sensations produced were so refreshing, stimulating and extraordinary, that not infrequently the habit was acquired without the victim realizing its dangers. It was for this reason that the habitual use of the drug was more prevalent among the section of population which was in the habit of chewing betel leaf. Some idea of its incidence could be formed by careful inquiries in towns where the habit was known to exist. The difficulties, however, in forming even an approximate estimation were great.

The incidence of the habitual use of cocaine during the period between the two world wars may be summed up briefly as follows : The areas which were most affected were the towns in Uttar Pradesh and southern Punjab, but the habit existed in the States of Bengal, Bombay, Bihar and Orissa. These could be put roughly under four categories : (1) large towns which were badly affected and in which the incidence of the habit was 5 to 10 per thousand of the population (e.g., Lucknow, Benares, Kanpur, Saharanpur and others); (2) large towns in which incidence was 2.5 to 5 per thousand (Mathura, Ghaziabad, Mirzapur and others); (3) smaller towns in which the habit existed to a small extent (e.g., towns of 20,000 to 40,000 where there would be 10 to 20 addicts); (4) those in which the habit had recently been introduced, and in which there were only a few addicts here and there.

The town of Delhi was about the worst affected, the incidence of the habit there being roughly 5 to 20 per thousand of the population during that period. A certain amount of addiction existed in towns in the neighbourhood of Delhi, chiefly among the artisan class in places such as Rohtak, Karnal, Panipat and Hissar. This could be attributed to rapid road communication brought in by the introduction of motor transport.

Investigation in the field in most of the states showed that in smaller towns and rural areas addiction to cocaine was almost unknown. Certain small townships and even villages in the neighbourhood of big commercial centres were sometimes affected, but not extensively.

III. Cocaine Traffic and Modes of Smuggling

For *bona fide* medicinal purposes, cocaine was imported into India from European countries, particularly from Germany, and later supplies were also received from America.

When restrictions on the sale and use of this drug were brought into force, a certain amount of the alkaloid began to be illicitly imported at first from the same sources. Later, the Far East drove the European and American manufactured article out of the Indian market. Japan, which manufactured the alkaloid, became the main source of supply for some time. Illicit cocaine was brought from Japan to Calcutta either direct or via Amoy by steamers of various lines. The conveyors were mainly Chinese, and to some extent Indian crew members, though acting independently of one another. Imports were managed through individual conveyors among the crew and not jointly.

China itself manufactured no cocaine, but imported it from Japan and Europe, and illicit traffic was carried on from its seaports through the ports of Hong Kong and Singapore, making use of various fictitious brands and labels.

The drug was hidden in inaccessible places in ships. On account of its small bulk, the landing of the drug did not present much difficulty. It was often not brought into the port at all in the ordinary way, but was thrown overboard in watertight packets into the sea or into the river from where it was picked up by organized gangs of smugglers. In this way, large quantities of the drug found their way into seaport towns such as Calcutta, Bombay and others.

The amount seized by the Calcutta customs authorities in 1930 was 7,200 ounces. Experienced excise officers placed the seizures at between 2 to 5 per cent of the quantity which actually got through. This meant that somewhere between 200,000 to 250,000 ounces of cocaine were successfully smuggled into the country every year. It was estimated by competent authorities at that time that consumers in India paid between 27 million and 65 million rupees to the retailers for their doses during 1929. This is an enormous sum of money, and from this some idea of the total number of persons addicted to the drug could be formed. Taking an average dose as 2 to 3 grains daily per individual, there must have been between 250,000 and 500,000 individuals who were taking cocaine habitually in India for its euphoric effects. This figure was very much on the conservative side, as a large amount of cocaine smuggled into the country was heavily adulterated by the dealers before it actually got to the consumers.

It is not necessary here to go into details of the devices which were employed by the smugglers. These have been dealt with by Mr. A. T. Bhargava of the Criminal Investigation Department in a pamphlet published by the Oriental Press of Allahabad in 1916, and can be added to indefinitely. It will suffice to say here that many extraordinary methods were used which enabled large quantities of the drug to be smuggled through into the hands of organized gangs in centres such as Calcutta. There was in existence a very elaborate system of distribution of the drug from the seaport to even the remotest towns in India. Depots had been established by the traffickers in towns where there was demand and which the retailers knew as a source of supply. Ordinary people in the guise of menials, such as grass-cutters, cobblers or labourers whom nobody would even suspect, were usually employed for transporting the drug. Sometimes purdah women in a " burka " * acted as carriers. Even respectable-looking Anglo-Indians and Europeans travelling first and second class in the railways were found in possession of large quantities of cocaine.

The distribution to the addicts was done chiefly through the agency of betel-leaf sellers, and also through itinerant pedlars. The police and excise authorities made a large number of arrests, causing the traffickers to become more careful. It being unlawful to possess or to sell cocaine, the traffickers did not carry it on their person, but placed the packets in some unfrequented place and indicated its location to the addict after they had received the price. The wholesale and retail dealers who kept stocks of cocaine were to be found in different towns and in many cases were known to the police. Actual arrest and prosecution were, however, very difficult, because the traffickers were clever in evading the law. They had effective methods of clearing away the drug at a moment's notice when their places were raided. The favourite method was to keep some water handy, and as soon as a police raid was anticipated the drug was thrown into water and the solution poured down the nearest drain, thus hiding from the police any trace of the drug. Carriers of cocaine were very rarely caught by the excise authorities. They carried only small quantities which could be easily concealed on the person. When bringing cocaine from big centres, these people often did not disembark from the train at big stations where they were likely to meet the excise agents. They frequently got out in small suburban or wayside railway stations and conveyed the cocaine by road to large towns. Even if some of them were arrested, they were paid well enough to go to jail and not give the chief culprits away. Very often, after doing a few months' hard labour, they came out and resumed their trade. Thus, the real persons who managed the business of smuggling not only escaped, but grew rich.

Betel-leaf sellers and women of low morals, such as prostitutes, played an important part in the spread of the habit to their clients. They were also sometimes the medium through which the drug was sold, and they induced their customers to buy and take the drug. A number of the addicts attributed the beginning of the habit to their association with these women.

Adulteration

It has been stated that the drug smuggled into the country was often already adulterated. The retail dealers further adulterated it with cheaper similar-looking products such as phenozone, acetyl salicylate, potassium nitrate, etc., the last-named because it imparts a sense of coolness to the tongue somewhat like cocaine. One consignment confiscated in Delhi consisted of pure phenozone. The drug was then put into small packets or " lifafas " containing $\frac{1}{2}$ to 3 grains (30 to 200 mg) each which were then handed over to the pedlars who were personally in touch with the addicts.

* The burka is an ample garment covering the body from head to foot (with a small aperture to allow the woman to see) under which even large packages can be carried unbeknown.

The Present Extent of the Habitual Use of Cocaine

It is not possible to form any idea of the incidence of the habitual use of cocaine in India at the present time. We have studied the figures of imports of cocaine from 1934 to 1957 very kindly supplied to us by the Central Board of Revenue. These do not show excessive import of this drug. The quantities imported are likely to be required for *bona fide* medicinal purposes in the country. Even if some of it was diverted illicitly for euphoric purposes, this quantity could not be large in view of the strict control exercised on its sale to the public.

We have also obtained figures of seizures of illicit cocaine from 1950 to 1957, the only figures available. Here also the quantities seized are very small. Granting that those seizures represent only 2 to 5 per cent of the cocaine actually smuggled in, as is estimated by excise authorities, the number of persons who use cocaine habitually for euphoric purposes could not be so large as to be alarming. There is no doubt, however, that the use of cocaine for such purposes does exist in India at the present time, small though it may be.

It is said that some cocaine is now being smuggled into the country from India's north-western frontiers, and if action is not taken this may become a menace. The opinion we have been able to form from our investigations is that eating of cocaine has not become extinct in India. The situation will have to be carefully watched by the authorities, as the remarkable and fascinating effects which the drug produces and the large financial gains it brings to smugglers may start illicit import on a large scale, and its habitual use may increase again.

IV. Analytical Study of 200 Cases of Cocaine Eaters

Two hundred cases of habitual cocaine eaters studied were collected not by selection from any particular area, but as they came during the course of work in the field. They were thoroughly examined and the histories, symptoms and physical and mental changes were recorded. The majority of this series, however, came from Delhi, and others from northern towns of the Uttar Pradesh and southern towns of the Punjab. The addicts were not seen just once, but with many of them — especially those from Delhi — it was possible to maintain contact for months, so that a more detailed and thorough study could be made. However, all of them were from the lower strata of society — that is, the artisan and menial classes. For obvious reasons it was not possible to get any of the wealthier class of people who indulged in the drug to come forward for examination. A number of them were of course seen, but detailed examinations and follow-ups were not possible. Even so, it was our impression that the better hygienic conditions, good food, etc., enjoyed by this class did not significantly mitigate the evil effects produced by the drug. On the contrary, we found that wealthier people who could afford to buy larger quantities of the drug deteriorated more rapidly. In them the process of physical, mental and moral degeneration was more rapid.

Race and Religion

The following is the division of the cases according to race and religion :

	Number	*Percentage*
Mohammedans	125	62.5
Hindus	68	34.0
Christians	4	2.0
Europeans	3	1.5
Total ...	200	100.0

It will be seen that the majority of our cases were Mohammedans (62.5%), followed by Hindus (34%).

The commonest age of contracting the habit in this series was between 15 to 30 years. The fact was obvious that the cocaine habit in India was chiefly the habit of the second and third decades of life, when the sexual functions were at their highest and sexual instinct dominated in the individual. In a small minority only was the habit started at a later period of life. There were a few cases in which the habit was formed as early as 15 or 16 years of age, showing that the drug was being conveyed to the teenagers in schools by pedlars. Between the ages of 16 and 40 years, the incidence was 79.6% ; between 40 and 50 years a few cases only were examined. It will thus be seen that in over 90% of cases habit formation occurred between the ages of 16 and 50 years. Cocaine eating in India would thus appear to occur mostly in the young. It begins with adolescence, reaches its maximum between the ages of 21 and 49 and declines rapidly as age advances. It is thus confined mainly to the period of life at which sex impulses are predominant — i.e., the sexually active or romantic period of life.

It was also obvious that prolonged and heavy indulgence in the drug adversely affected the longevity of the addicts, and many of them did not live much beyond the age of 40.

The majority of addicts in our series were of the artisan class : shopkeepers, taxi drivers, tradesmen and the like who made a modest living. The rest came from practically all classes, but chiefly the menial classes. They spent most of their earnings on the drug. More than 60% of the addicts were unmarried. This, in a country like India, is a high percentage. The series was not large enough to permit any conclusions to be drawn as to the effect of the drug on fecundity.

Sex incidence

Only seven of this series were females. This, however, does not reflect the true sex incidence, as most of the women who take the drug would naturally not come up for examination in this country. In the Uttar Pradesh area at least, many women were known to be taking the drug at that time.

Dosage

In more than 45% of the cases the dose did not exceed 1 to 2 grains daily, in 21% between 3 to 4 grains, and in 24% between 5 to 10 grains daily.

V. Aetiology of Cocaine addiction

(1) *Association*

In India, the use of cocaine was to some extent confined to the class of individuals who were more or less addicted to other narcotic drugs such as opium and " ganja ", or to alcohol; but it was also met with in people who were not using any of the other narcotic drugs. The chief cause of the habit was association with cocaine eaters or people who were taking other narcotic drugs. It is a curious fact that people addicted to euphoric drugs always attempt to persuade their friends and acquaintances to try the drug of their choice. We have known cases where betel leaf with cocaine was given to individuals without their knowledge, and resulted in their becoming habituated to it. Many of the older addicts said that their first introduction to the drug was by traffickers who told them of its remarkable effects. They were given the first few doses gratis and when they had enjoyed the effect and were attracted by the drug, they ended up by spending all their money in buying it.

Others try the drug out of sheer curiosity. A small number underwent such severe reactions after taking the first dose that the experiment was not repeated. Others, however — generally the class of individuals whose mental equilibrium was not stable — obtained such pleasurable effects, temporary though these were, that they almost invariably bought the drug, repeated the dose, and in this way became victims to the habit. Inexperienced youngsters fell into the habit of taking the drug, and their whole life was ruined. Cases are known of boys who contracted the habit through the agency of their household servants or some designing person, with disastrous results.

(2) *For its Pleasure-giving Effects and as a Luxury*

Cocaine eating in India was more or less confined to people with licentious and vicious habits. Sexual vice and dissipation being very prevalent in these circles, they were always anxious to find new avenues of pleasure-giving sensation. Those belonging to the indolent rich classes took the drug because their sense of appreciating the ordinary pleasures of life had become dulled or exhausted, and they wanted some sort of stimulant so as to be able to enjoy again the pleasurable sensations to which they had become insensitive through long and excessive indulgence. This type of individual was not rare in large towns even among the artisan classes. The surroundings in which these people worked were dull and unhygienic, and they took to narcotic drugs for want of healthy recreative occupations. There was also the idle rich class already referred to who, having no occupation, started taking euphoric drugs for the sake of " having a kick out of life " or " to make it worth living ".

(3) *For Sexual Gratification*

Cocaine is one of those drugs which was frequently used by the women of the underworld and prostitutes in India not only for their own pleasure, but also for stimulating the sexual appetite of the licentious people who visited them. The pleasurable sensations produced by the drug stimulated their sexual desires. The temporary stimulation of the psychic areas probably produced mental excitement resulting in a semblance of aphrodisiac effects in some individuals. This was certainly the case with the female sex.

(4) *To alleviate Fatigue, Worry and Strain*

Since cocaine removes for a while the feeling of fatigue and hunger and gives a feeling of self-satisfaction and forgetfulness, it was sometimes taken by some working-class people towards the evening after the day's work. As the effect of one dose lasts for only a short time, the desire to repeat it at frequent intervals became irresistible in some of them.

(5) *Disease*

This was a very rare cause for contracting the habit in India; in our series of 200 cases there were only two addicts who started the drug because it relieved attacks of asthma from which they were suffering and for which they first took the drug.

(6) *City Life and Cocaine Addiction*

Cocaine eating in India was chiefly confined to dwellers in towns and cities. Insanitary conditions, overcrowding, want of hygienic and healthful recreation, the strain and stress of life in large towns, all predispose to addiction to euphoric drugs. The cocaine habit was practically unknown in the rural areas not only because of the non-availability of the drug but because people's time was fully occupied with work. The economic condition of these people did not allow them to spend their hard-earned money on such an expensive drug. Besides, there was the fear that in a small community such a habit would soon be known to others.

(7) *Nervous and Psychological Factors*

The cocaine habit, like other narcotic drug habits, is chiefly confined to individuals whose psychic condition is in an unstable state of equilibrium. Most of the addicts examined could be put in two classes : (*a*) Weak-minded, phlegmatic and mentally dull and deficient individuals; there might have been a family history of insanity, alcoholism or neurosis in such cases. These individuals were unable to stand the daily stress of life and often resorted to drugs to enable them to carry on their daily routine of work. Such individuals did not resort to cocaine for sexual or vicious purposes, but merely for its stimulating and euphoric effects. In our experience with opium addicts, this was a common cause of contracting the habit, and we have no doubt that this factor also played an important part in habitual use of cocaine in India. After a dose of cocaine, persons who were irritable and depressed became self-confident and cheerful and were able to face the world with fortitude. Unfortunately, the effects were temporary. (*b*) Irritable, nervous and hypersensitive temperaments. Such individuals formed a smaller group. They became easily upset and irritated by small worries of life of which normal persons would take no notice. They wanted some sort of sedative or narcotic to give them a sense of mental balance.

Methods of taking Cocaine

The method almost universally employed in India is by putting the drug in " pan " (prepared betel leaf). This was the reason why addiction to cocaine was more prevalent amongst people who indulged in " pan " chewing. As is well known, the betel leaf is taken by mixing it with small quantities of catechu and slaked lime; a little betel nut or sometimes spices such as cinnamon, cardamon, ginger, etc., are also added. Cocaine is either mixed with the spices and then wrapped in the betel leaf, or some of the eaters place the alkaloid on the tongue and then chew a " pan " immediately afterwards. Habitual cocaine eaters who have been indulging in the drug for a long time generally put the cocaine on the tongue and merely take a little lime and catechu afterwards, dispensing with the betel leaf altogether. It is said that by doing this the action of the drug is enhanced and the effects produced are stronger. Rarely, the drug has been taken in the form of a solution, obtained on a doctor's prescription, the addict sipping the solution at intervals and following it each time with a betel leaf. The method of rubbing the drug into the gums or taking it as a snuff is up to the present time unknown in this country, and we did not meet anyone who used it this way. A method occasionally employed — particularly by prostitutes — is that of injecting a solution of cocaine into the vagina by means of a douche. This give the individual a sense of local constriction and general effects appear almost immediately. The sexual act is said to be prolonged if the drug is administered in this way.

VI. Symptomatology of Cocaine Addiction

From a careful study of 200 cocaine eaters it has been possible to form some idea of the symptoms and effects produced by the drug in Indian addicts. A description of the symptoms produced was obtained first-hand from the cocaine eaters themselves and is reproduced below.

Immediately after taking the drug there is a slight smarting or tingling sensation in the tongue; the lips feel swollen, dry and thick. There is irritation in the fauces and a sensation of constriction in the throat. Soon there is a complete loss of sensation in the oral cavity, tongue and lips. There is a feeling that the tongue is missing from the mouth. Following these preliminary sensations, which last less than ten minutes, the drug begins to gain entrance into the circulation, and the stimulant stage begins. There is a slight feeling of dizziness or heaviness in the head, a throbbing sensation in the arteries of the neck and palpitation of the heart. The unpleasant sensation of confinement and air hunger, which sometimes occurs after subcutaneous injections of cocaine, is rarely met with when the drug is taken by the mouth, unless the saliva is swallowed or enters the stomach by trickling through the oesophagus. There is a very pleasant sensation, a feeling of warmth all over the body, and sensation that something is being drawn away from the limbs towards the head and the mouth. A peculiar, delicious feeling is perceptible in the region of the tongue. The ears become hot and red, the cheeks become pale, the tip of the nose becomes cold, and the patient begins to perspire on the forehead and over the neck. These symptoms are more common in the early stages of the habit, but are hardly perceptible in confirmed cocaine eaters of long standing, unless they take an overdose.

By this time a peculiar sensation of excitement is felt by the individual; he feels cheerful and experiences a sensation of comfort both in mind and body. He feels capable of undertaking anything, however difficult, whether it may involve physical or mental effort. During this period the cocaine eater looks very keen and excited, his eyes are bright and he talks coherently. Complicated intellectual work may be done without mistakes. The increased sensitiveness of the sensory nerves is perceptible all over the body. The eater gets agreeable hallucinations, he imagines himself to be a wealthy man such as a rajah or a nawab. During this stage he may walk along the streets continuously for hours without feeling fatigued. His eyes may be glued to the ground and he imagines he is looking for gold and treasures; instead he picks up rubbish, stones and other articles from the ground thinking them to be riches and articles of value. These he carries on his person till he recovers from the effects of the dose and finds them to be useless. During this time he is afraid of being robbed and fears everyone he meets. Fear of excise authorities or the police are prominent among the hallucinations occurring among the poorer class of addicts in India. The indication of the maximum amount of exhilaration is marked by coldness of finger-ends, and mydriasis.

When chewing the betel leaf, cocaine eaters as a rule have marked objection to talking. As the leaf is chewed the mouth becomes full of saliva, and there is a pleasant sensation as if the whole cavity were full of butter which spoken words might dissipate. The addicts as a rule do not swallow the saliva but retain it in the mouth and give it time for absorption from the buccal cavity. The reason for this appears to be that if some of the saliva containing cocaine gets into the oesophagus and from there into the stomach, it gives rise to a feeling of constriction and discomfort in the throat and chest. Besides this, the drug is more quickly absorbed from the stomach and produces a more intense action which in the uninitiated may be so severe as to produce symptoms of great discomfort all over the body and even a mild collapse. Ordinarily these symptoms consist of a sense of confinement in space, lack of air, feeling of severe oppression in the chest, dizziness and heaviness in the head. The saliva is not swallowed, in order to escape from the concentrated effects of the drug. In order to avoid its trickling into the gullet and stomach the addicts firmly close their lips and avoid talking to friends when they are chewing the betel leaf containing cocaine. Confirmed and experienced cocaine eaters, however, do not hesitate to swallow the saliva to get stronger effects from the dose. Those who are new to the drug and are afraid of its strong effect expectorate the saliva when chewing the betel leaf.

The stage of excitement after cocaine lasts from forty-five minutes to about two hours. There was a good deal of difference of opinion among cocaine eaters regarding the duration of the stimulant stage, undoubtedly due to the fact that most

of the drugs supplied was adulterated to a greater or lesser extent. The addicts who had been taking cocaine for long periods were sure that the pure drug which they formerly obtained had a much stronger and lasting action than the adulterated commodity they obtained later. The effects, they emphatically stated, certainly lasted for one hour to about two hours or even longer. They also said that in six months the pure alkaloid reduced the eater to a state of a physical and mental wreckage when large doses were taken. He became pale and thin " like a straw ", as many of them described the condition. The intoxication effect of the heavily adulterated drug (according to the majority of them) did not last for more than an hour or two.

During the stage of excitement, the cocaine eaters like the company of other eaters, and they mutually persuade each other to indulge more and more in the drug, thus leading to long cocaine debauches. The advanced hours of the night do not induce them to retire to sleep, as during cocaine intoxication the sensation of fatigue and drowsiness is entirely absent. In this respect cocaine differs from other euphoric substances such as opium, cannabis preparations or alcohol which sooner or later produce drowsiness and sleep. Many cocaine eaters related how, when indulging in cocaine, they sometimes did not sleep or even close their eyes for two or three nights. When, however, the debauch was finished and the effects of the drug had passed off, they experienced the results of their vigil in the form of an acute feeling of physical and mental fatigue, headache and extreme misery, till they dropped into natural sleep from sheer exhaustion. If a fresh dose of the drug is taken, even at this stage, it has a wonderfully reviving effect, the eater feeling more or less normal for the time being and capable of doing any kind of work. The resultant depression is much greater, because there is an irresistible desire to repeat the dose again and again in order to get over the loathsome depression which follows. When the drug is available, sueh doses may be repeated many times, and deaths have been recorded from cocaine poisoning on account of over-dosage. If another dose cannot be obtained, the cocaine eater feels absolutely lifeless and dejected and prefers to be left alone. He has a sensation of impending death.

During the stage of depression the eater experiences a strange fear of unpleasant happenings, and persuades himself to take a fresh dose to get over this. The depression of spirits, however, seems to be more imaginary than real, for there is no fall of temperature, no effect on the pulse, heart or respiration. The tongue and lips become moist again, the perspiration on the forehead and neck stops altogether. During this period, the cocaine eater avoids the company of his friends and associates, and has a feeling of hiding himself away from them and people in general. He may lie down in a quiet, dark corner refusing to speak to or even to face his friends. During this stage also the cocaine eater may sometimes suffer from maniacal symptoms such as hallucinations, chiefly taking the form of persecution by the police or excise authorities. He imagines that the police are coming in search of him, and any noise or sound of footsteps startles him.

A large number of cocaine eaters are subject to paraesthetic sensations such as formication and crawling of insects or snakes or lice on the body or under the skin. Others get intense itching all over the body. A number of cases of insanity have followed a prolonged period of cocaine eating. While the individual is under the influence of cocaine, there is complete loss of appetite. There is no desire for food at all, and a cocaine eater will reject the daintiest dishes offered to him during this period. Often a very intense feeling of thirst is experienced.

Cocaine eaters suffer from a very obstinate type of dyspepsia which is believed by them not to yield to any other form of treatment except another dose of cocaine. On account of its stimulating effect on the ganglia of Auerbach's plexus, a dose of the drug in many eaters produces rapid evacuation of the bowels immediately after it is taken. This symptom was particularly noticeable in cocaine eaters of the Delhi area. Soon after taking the dose they had to run to the latrine, where they remained seated for a considerable time absorbed in their delusions. Constipation, however, is more common, and it is the most distressing sympton occurring in cocaine eaters. It was given by many as the reason for the repetition of the dose. It was said that the bowels were confined, and there was a very unpleasant sensation of fullness in the abdomen — the feeling being described as if the inside was full of stones. This was readily relieved by a dose of the alkaloid, the effect being so strong that a rush had to be made to the lavatory immediately after the drug was taken. Some cocaine eaters of old standing, however, were not worried much by either the constipation or other gastro-intestinal symptoms.

Another distressing sympton noticed in cocaine eaters was insomnia. They kept awake all night desiring a fresh dose of the drug. They simply could not sleep although they tried very hard. The ordinary hypnotic drugs appeared to produce little or no effect in producing sleep. Most of the cocaine eaters complained of insomnia, and it was very often for this reason that they consulted a doctor. In a few of the addicts who took fairly large doses, insomnia did not occur. Delusions and hallucinations greatly disturb the mental equilibrium of cocaine eaters and gradually make them very miserable. The prolonged use of the alkaloid is also said to bring about deafness, and confirmed cocaine eaters are said to be often slightly deaf. This was observed in a number of subjects studied by us.

Toxic Effects

In the case of stronger intoxication, whether through bigger doses or abnormal sensitiveness of the individual, hallucinatory symptoms quickly appear. These hallucinations (as already stated) are of the nature of persecution and paraesthesia of the skin. Sometimes, especially after larger doses have been taken, there is a feeling of sickness, nausea, vomiting and cramps in the muscles. If toxic doses of cocaine are taken, the eater may become semi-conscious and may suffer twitchings of the muscles of the face. General tremors of the body may occur, followed by convulsions. The body temperature shows a considerable tendency to rise. Convulsions can be

easily controlled by sedatives and, if severe, inhalations of a general anaesthetic may be necessary. Very often they pass off, the patient gaining consciousness but feeling utterly exhausted and miserable. A dose of cocaine in this condition revives the victim almost immediately. Paralytic symptoms may appear if very large doses of the drug have been taken. This may be followed by coma and death from stoppage of respiration. These, of course, are extreme cases of intoxication, and are very rarely seen.

Abstinence Symptoms

The foremost of these is a strong desire or a craving of the cocaine eaters to repeat the dose. After the effect of one dose is over, the desire for the next dose is almost irresistible. The one idea in the addict's head is to get another dose, and he will do anything to satisfy this craving. There is such a strong desire in some individuals for the drug that the eater will commit any kind of crime, and a woman will even sell her honour to get the drug. The eater feels restless, irritable, unable to concentrate, and quarrelsome. There is a great disinclination for mental and physical exertion, and he feels dull, drowsy and lazy. In fact, he is in a condition of complete lethargy and inertia; the gastro-intestinal functions are depressed; sometimes the symptoms of constipation, cramps and sensation of formication, etc., are delayed, not appearing for three to four days after the debauch. Rarely patients get so depressed that they feel they are going to die; they may become prostrated and may collapse. Such symptoms are met with much less frequently in the case of cocaine than with opium and morphine. A number of addicts, especially those taking large doses, lose all interest in their life and surroundings and develop suicidal and morbid tendencies. All these symptoms disappear for a while if a dose of the drug is taken.

Time of taking the Drug, and Dosage

Cocaine is generally taken by the eaters in India late in the evening or in the early hours of the night. Persons engaged in dissipation, who are confirmed and inveterate eaters, take it during all hours of the day in betel leaf. It was noticed that many of the artisans and workmen in Delhi did not take the drug except once during the evenings when they had finished their day's work. Others took it twice a day and no more. They generally took one or two doses of the drug or as much as they could afford, and then went home to rest. They said the effect of one dose lasted them for six to eight hours, and if they could get it they were able to carry on their daily vocation without any difficulty. Occasionally, however, some went on taking small doses of the drug all night, especially when they were in the company of prostitutes.

Dosage. The daily dosage consumed showed wide variations. The drug was very expensive and difficult to get; besides, it was often very heavily adulterated. The tendency to increase the dose was strong, and in the short space of a few weeks the dose was sometimes increased to 20 or 30 grains a day. Rich people as a rule were apt to take much larger doses than people with smaller means. The majority of the eaters took doses ranging from a half grain to 15 grains, the latter being the maximum limit among the ordinary type of eater. There were, however, exceptional cases where individuals were known to have taken as much as 60 grains in the course of a single night.

Physical Effects

Cocaine addiction is a disease like other addictions, artificially produced by the individual himself. It has already been stated that neuropathic diatheses, neuroses, worry, exhaustion and mental instability or deficiency all act as predisposing factors to this drug habit. The addicts were in the majority of cases individuals with an initially unstable mental equilibrium. Cocaine being a general protoplasmic poison, it acts detrimentally on all the tissues of the body, particularly the nervous tissues. The habit undoubtedly leads to a state of chronic toxaemia. There are two types of poison concerned in producing a toxaemic state in cocaine eaters. These are :

(*a*) *The exogenous poison* — that, is the drug itself — which is absorbed from the mucous membranes of the mouth and pharynx and then circulates in the blood.

(*b*) *The endogenous toxins* which are formed by the action of the alkaloid on the general metabolic processes of the body and the biochemical changes thereby set up.

Both these factors combined interfere with the normal functions of the organs, giving rise to debility and anaemia. General toxaemia and improper assimilation of food lead to general wasting, sallow colour, anaemia and finally a cachectic condition.

General Appearance of Cocaine Eaters

The general appearance of cocaine eaters is very pitiable. It is not difficult to recognize them when one has seen a few. They are as a rule emaciated, sickly and flabby-looking individuals with a dull facial expression. They have no regard for personal appearance or cleanliness of body or clothes. They are pale and anaemic, have a sallow complexion, sunken eyes, dilated pupils, prominent cheeks, and look as if they are suffering from severe toxaemia.

When not under the influence of the drug, the cocaine eater looks a picture of misery. In the vast majority of eaters there is a blackish-red deposit on the teeth. This is said to be a very important sign in cocaine eaters in India and by some is regarded to be pathognomic. The usual colour of " pan " in the mouth is red on account of the catechu contained in it; the colour of the teeth and tongue of cocaine eaters is, however, dark brown or chocolate. The teeth appear stained with a dark reddish or black coloured deposit, and the tongue is also coated with dirty, dark coloured fur. Both these conditions are attributed to the fact that cocaine eaters do not pay any regard to the cleanliness of the mouth and teeth; the tongue therefore becomes very dirty. It is also possible that owing to the anaesthetic effect of the drug on the mucous membrane of the tongue, the cocaine eaters use much more lime in the " pan " than if the mucous membranes were

sensitive. Many of the addicts have cracked lips, due probably to the irritating effects of the lime and the devitalizing action of the alcaloid on the various parts of the oral cavity. The parts become insensitive and, therefore, any mechanical or chemical injury is not readily felt and is aggravated. The coloration of the tongue and the teeth does not disappear even a month after the eating of the drug has been given up. The black deposit is more marked on the lower teeth, particularly on their posterior surfaces. It is more in evidence on the central incisors and canines, but not infrequently it extends to the last molar teeth. There is no doubt that this deposit is due to chemical changes taking place between lime, catechu and the alkaloid in the alkaline medium of the saliva. Those who wash out their mouth immediately after they have taken the " pan " with the drug as a rule do not have these deposits to the same extent. This dark red colour of the teeth and tongue is one of the signs by which cocaine addicts can be recognized in India. Some people, however, use a preparation called " missi " which gives a black colour to the teeth very similar to that of cocaine.

Gastro-intestinal Symptoms

Cocaine undoubtedly has a well-marked toxic action on the digestive system. It has already been pointed out that habitual cocaine eaters suffer from persistent loss of appetite due to the dulling of the sensibility of the mucous membrane of the stomach. They take very little by way of food and drink, and can do without any nourishment for days when they are taking the drug. This naturally interferes with the nutrition of the body, and produces emaciation and wrinkling of the skin. It was observed that individuals who were strong, robust and handsome became pale, emaciated and dark, and looked physical wrecks in the course of time. Some of them were reduced to mere skeletons. Sometimes, but rarely, cocaine eaters have a craving for eating earth. Owing to the stimulant action of the drug on the sympathetic system, cocaine eaters generally suffer from relaxed condition of the tone of the intestinal musculature. It is this which produces the obstinate constipation and stasis of the gut contents leading to toxaemia, which has been described above (p. 19).

Circulatory and Haemopoictic Systems

Stimulation of the sympathetic nerves and ganglia in the heart gives rise to palpitation and acceleration of the pulse rate. The pulse becomes full and its frequency does not, as a rule, exceed 115 per minute. After the dose, the blood pressure usually rises and there is a throbbing sensation in the arteries of the neck and the blood vessels look full. When the stimulant effect of the dose is over, the pulse generally shows some slowing. Auscultation of the heart immediately after a dose reveals increased frequency and force of the heart beats. In anaemic persons, murmurs may be heard. Besides this the alkaloid, especially in large doses, has a toxic action on the myocardium, and in old-standing addicts and those taking large doses the pulse is weak and the blood pressure low. Even after moderate doses there is stimulation of the sympathetic nerves and depression of the vagus, but after the stimulation there is generally a paralytic condition of the sympathetic system.

As regards the effect of cocaine on the haemopoictic system, there is little doubt that the drug has a direct action on the blood-forming organs, especially when taken in large doses. It also produces an indirect action by producing intestinal stasis and toxaemia and through the malnutrition it brings about.

Respiratory System

Soon after taking the dose the respiration is quickened. When large doses are taken there is marked quickening at first, the respiration becoming deeper and more frequent. This effect is undoubtedly produced by the stimulation of the respiratory centre. With toxic doses there is a slowing down, and the respiration may assume the Cheyne-Stokes type.

Genito-urinary System

The amount of urine in cocaine eaters is said to be diminished, but we have not been able to carry out any observations on that point. Probably this is due to a smaller intake of both food and drink. The urine of a number of eaters in this series did not show any abnormal constituents; the quantity of the alkaloid, if it is excreted by the kidneys, is probably too small to be detected by the ordinary alkaloid-precipitating reagents. None of the addicts complained of passing abnormally small quantities of urine, but tenesmus of the bladder was observed, especially after large doses. Women taking cocaine habitually suffer from backache, leucorrhoea and often from amenorrhoea and dysmenorrhoea.

Nervous System and Sensory Organs

The central nervous system is the greatest sufferer from cocaine eating, the highly developed nerve cells of the grey matter suffering most of all. These cells are at first violently stimulated, and the stimulation is followed by a reactionary depression. The effects, such as delusions, hallucinations, impairment of character and low state of mental efficiency and sometimes a sort of chronic insanity called " cocaine paranoia ", can all be thus explained.

We found that prolonged use and excessive indulgence lead to great mental impairment, and a drift towards insanity. We observed a few cases of epilepsy, the fits having started after the commencement of the habitual use of the drug. Some addicts suffered from suicidal and homicidal impulses, the former being more common. All these effects are no doubt brought about by the persistent use of the drug resulting in structural changes in the nervous tissue. The most distressing of all symptoms was insomnia of a very obstinate nature.

There may be widening of the palpebral fissure and the cornea may have a glassy appearance. The eyeballs also protrude, owing to sympathetic irritation. In two of our cases at least there was impairment of vision and hearing was generally impaired. The deafness occurring among cocaine eaters was probably due to the paralysing effects of the alka-

loid on the auditory nerve endings. The superficial and deep reflexes were not affected. The skin was pale, there was loss of subcutaneous fat, and in some cases a peculiar rash was observed. Paraesthesias were frequently met with (in 30% to 40% of addicts in this series). The paraesthesias appeared and disappeared.

Sexual Effects

Cocaine has the reputation in India of being perhaps the most important euphoric drug to be associated with the stimulation of sexual functions. For this reason it is closely associated with sexual vice and prostitution. Quite a large number of this series started the drug for its alleged stimulating effect on the sexual faculties. On careful questioning, however, none of the cocaine eaters could say definitely that the drug possessed any marked stimulant effect on the sexual faculties and appetite. During the general stimulation of the higher parts of the brain which follows indulgence in this drug, there is undoubtedly sharpening of all the senses and faculties and this may produce a semblance of sexual stimulation. Even in this state the alkaloid has no specific exciting effect on the sex organs either in the male or in the female. It has been stated that the period leading up to ejaculation is greatly extended in man, but most cocaine eaters said that the sexual act was not in any way strengthened or prolonged; as a matter of fact, most of them said that it was distinctly weakened. When deeply under the effect of the drug, cocaine eaters said it was impossible to perform the sexual act. It was during the depression period that, according to some of them, the act was considerably strengthened and the ejaculation time markedly extended.

As regards the effect of the drug on the female sex, data in this respect have been very limited, being confined only to a few prostitutes. In his able memoire on cocaine addiction, Professor Hans W. Maier (1926) stated that owing to the stimulation of the psychic areas, bodily erotic attractions increase in those who are inclined that way. Habitual use of cocaine in such individuals generally has a sexual origin, and the users show all possible perverse symptoms and loss of moral control. Homosexuality is not uncommon amongst those indulging in the drug, and this was actually observed in some cocaine eaters of Uttar Pradesh. Sexual depravity is undoubtedly due to loss of control of the higher centres which is present under normal conditions and is absent in cocaine eaters. Hetero-sexuality may change to homosexuality during intoxication. It was definitely stated that the sexual desire certainly increased among the female cocaine eaters.

A number of cocaine eaters stated that cocaine has a distinct depressant action on sexual functions in all stages. A few said that in the beginning the sexual act was somewhat prolonged but a distinct weakening effect was produced later on in the course of its habitual use. Others stated that they felt no sexual desire while under its influence, but the desire returned after its effect had passed off and then he or she experienced voluptuous feelings. Still others definitely stated that they did not get erections while under the effect of the drug, their only desire at that time being for a fresh dose. These people felt sexually fit only when the intoxication produced by the drug had entirely passed off.

It would be interesting to note here that not a few of the cocaine eaters, especially those who had taken the drug for a long time, complained of sexual neurasthenia and complete loss of sexual desire and disinclination for the company of the opposite sex.

Social and Moral Effects

Cocaine eaters are generally despised in India. The cocaine eater, contemptuously called " cocaine baz " (one indulging in cocaine) is intensely disliked by those round him. It was noticed that almost all cocaine eaters were persons of low morals and that they were habitual liars and pilferers. No one would trust them in business matters, and their evidence in court was not relied upon. Their company was considered to be objectionable by their neighbours and relations. They had lost all sense of self-respect and would resort to anything, however despicable or criminal, to secure their daily dose when it was not forthcoming by fair means. Some of them said that they would simply take the dose from another by force if they could not obtain it by other means. It has been stated that the reason why cocaine among all other narcotic drugs deserves the fullest attention is first, the easy way of its application (i.e., by eating in " pan "); secondly, because the drug is not indulged in isolation by the addict like some of the other narcotics — it is taken in company and its use spreads like a contagious disease; lastly, its disintegrating and demoralizing effect on the character of the individual paves the way to prostitution and crime.

The cocaine eater in India, so far as it can be judged from this small series, is more dangerous to himself than to other members of the society from a criminal point of view. Many cocaine eaters of the artisan class observed by us carried out their daily vocations and indulged in the drug only in the evening for an hour or two, afterwards returning to their homes or spending the night in the company of some women. They took the drug, they said, just to experience the exquisite feeling produced by it. When asked to describe what sensation they felt, they said that they could not describe it in words, just as they could not describe the sensation of pleasure obtained during the sexual act. They all said that the sensation was so wonderful and fascinating that they were prepared to face all consequences to obtain it even for a short space of time.

A number of cocaine eaters said that they repeated the dose of the drug because of the severe constipation from which they suffered, and because of the most distressing feeling in the abdomen, which could not be relieved except by a dose of cocaine. They all loathed the habit and wished to be rid of it. They begged us to find something which would help them to conquer the craving. They all remembered their first introduction to the drug and cursed the person who was responsible for introducing them to the habit.

Strength of the Habit

The cocaine habit once formed is very difficult to give up, although it is believed by some to be not more difficult to abandon than the opium habit. Prolonged use leads to mental deterioration and weakness of will power, so that the individual seldom has the strength to give it up. The withdrawal symptoms already described, especially insomnia, cramps in the muscles, constipation, disturbance in the abdomen, etc., make it all the more difficult. Proper guidance, complete removal from the environment and improvement of the physical condition and vitality of the patient may help him to resist.

VII. Diagnosis and Treatment

In India it is not difficult to diagnose cases of cocaine addiction after one has seen a few eaters. The following are the chief points which help in diagnosing a cocaine eater.

(1) The general appearance of the addict : he is generally young, emaciated, with sallow complexion, sunken eyes, wrinkled face and dilated pupils.

(2) The dark, chocolate-coloured deposit on the teeth and the tongue. (This deposit is more marked on the incisors and canines, particularly on their posterior face.)

(3) Such symptoms as hallucination, delusions of a persecutory nature, moral and mental degeneration.

(4) Paraesthesias.

Treatment

The treatment is general. The most important points to be remembered are :

(1) Removal of the cocaine eater from the environment in which he indulges in the habit, and from the associates in whose company he takes the drug, preferably to a place where he cannot get the drug. This is very important. We have known instances where individuals went from Delhi or Saharanpur for a few months to the Punjab where they were unable to get the drug and where they had no associates. They conquered the craving for months without much difficulty. When, however, they returned to their old surroundings (where they were able to obtain a supply of the drug) they again succumbed to the temptation. Similar facts have been observed in cases of cocaine eaters who were sent to prison. The habitual use of the drug was given up in goal without difficulty for years, but immediately on release the use of the drug was started again.

(2) Psychotherapy, mental training and impressing upon addicts the gravity of continuance of the cocaine habit are very important.

(3) The drug must be withdrawn all at once.

(4) The rest of the treatment is simple and symptomatic.

Cramps and insomnia should be treated by simple means such as massage, exercises, hydrotherapy (warm baths). If there is need for a sedative, bromides should be given; chloral and paraldehyde should be used with caution, while hypnotics such as opium and morphia are absolutely contra-indicated. General tonics such as iron and strychnine and vitamins should be given. Quinine, strychnine, iron and arsenic in pill form are very useful. Constipation should be treated by simple means such as warm soap enema or saline purgatives. Drastic purgatives are not recommended.

Diet should be simple, easily digestible and nutritious, such as milk, soups, vegetables (minced and well cooked), and fruit juices. Farinaceous vegetables and fats should as a rule be avoided in the early stages of treatment.

VIII. Summary

(1) *Erythroxylon coca* has never been cultivated in India on a large scale. So far as is known, no other varieties of *Erythroxylon*, which bear cocaine, grow wild in India or are cultivated. The leaves of *E. coca* have never been used in India for euphoric purposes.

(2) The use of cocaine for euphoric purposes is of comparatively recent origin in India, the earliest records of its use being less than a hundred years old.

(3) During the period between the two world wars habitual use of cocaine in " pan " (prepared betel leaf) became a serious menace in the towns of certain states of India. The evil effects produced came to the notice of the medical profession and the authorities. Severe restrictions were at once placed on the import, sale, possession, transport and use of the alkaloid and the preparations in which it was contained and ecgonine from which it can be manufactured. In spite of this, the habit spread from Calcutta to large towns along the two main railway routes through the Uttar Pradesh into the Punjab and the North-West Frontier. From Bombay it spread to some of the large towns in that state.

(4) Cocaine was smuggled into India in large quantities from the Far East through seaports, particularly Calcutta. It was illicitly brought by crews of various lines of mercantile marine from the Far East, especially Japan, where it was manufactured. It was distributed to different parts of the country by smuggling organizations, through a network of pedlars. Smuggled cocaine was generally very heavily adulterated, the chief adulterants used being phenozone, phenacetine, caffeine citrate, acetyl salicylate and potassium nitrate.

(5) The habit of cocaine eating was chiefly prevalent among the betel leaf chewing population of the north western region of India (including the States of Bengal, Bihar, Uttar Pradesh and, to a lesser extent, the Punjab). It was estimated that about half a million cocaine eaters belonging to different strata of society existed during the period between the two world wars. The habit was foremost among the artisan class in large towns.

(6) With regard to the present extent of cocaine eating in India, it is not possible to form any idea. The legal imports of cocaine from 1934 to 1957 as well as the seizures of illicit imports indicate that the use of cocaine for euphoric purposes is not large, but there is no doubt that it does exist.

(7) Two hundred cocaine eaters were examined and studied. Analytical data are given regarding the causes leading to cocaine addiction; its duration; the occupation of the

addict; the dosage; the sex incidence; its effects on sexual functions; its association with other drug habits, etc.

(8) The main causes leading to cocaine addiction were association with other eaters (66% of cases in this series); luxury and pleasure (21%); fatigue, worry and strain (6.5%); curiosity and fancy (4.5%) and disease (2%). The habit is chiefly confined to individuals whose psychic condition is in an unstable state of equilibrium.

(9) The most common method of taking cocaine in India is by putting it in a " pan ". The drug is either mixed with spices, which are usually put in " pan ", or some of the addicts place the alkaloid on the tongue and then chew the betel leaf afterwards. Addicts of long standing generally put cocaine on the tongue and follow it up by a little lime and catechu, dispensing with the betel leaf. This is believed to enhance the action of the drug. The method of taking the drug by injection or taking it in the form of snuff is unknown in India.

(10) The symptoms produced in cocaine eaters as observed in the small series of 200 cases are described in detail. The deleterious effects of the habit on the physical, mental and moral condition of the addict are discussed.

(11) The diagnosis of cocaine addiction and its treatment are described.

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Care and treatment of drug addicts

By Kenneth W. Chapman, M.D.

Origins of Addiction

The reasons for drug use are widely variable and include not only individual and social differences but other determinants such as culture, economics, and individual health states, both physical and mental.

In some eastern countries, for example, the average rural villager has no medical personnel, no one to turn to in illness, and no relief from pain but opium either smoked or eaten. The chronically ill are easy prey to such drugs. On the other hand, it is not unknown in western countries for physicians carelessly to administer narcotics and through neglect cause a patient to become an addict.

It is probable that through personal interest, association, or group pressures many individuals become acquainted with the drugs and find in them a pleasurable sensation which they try relentlessly to recapture.

For half a century or more discerning students of addiction have recognized that drug addiction is only a symptom of an underlying personality and/or emotional disorder reflecting the inability of the individual to adjust to life without narcotics rather than a specific disease entity peculiar to that individual. The remarkable characteristics of the opiates, in particular, in reducing anxiety related to fear of pain, hunger, or sexual urges without seriously impairing the senses make them a suitable substance for relief from emotionally conditioned pain.

The passive-aggressive may find in opiates needed support for his weak ego defences. The magical thinker finds brief escape from reality in the world of fantasies through drugs. To certain " acting out " individuals, the taking of drugs may express their hostility both towards hated parents and their social surrogates. These by no means exhaustive examples will serve to indicate the breadth and complexity of the individual personality problems leading to drug addiction.

Other intimate problems of the individual play an important part in many circumstances. Frustration in some members of minority groups may be relieved through drugs. Hunger may be assuaged by narcotics. The use of opium by overworked parents to quiet their hungry or troublesomely active children is a recognized factor in several countries.

The prevailing attitudes of the cultural and social milieu will also play a part in the development of addiction as well as influence the psychiatric factors. For example, opium smoking acceptable within certain subcultural groups of the Asiatic continent provokes little, if any, anxiety in its habitués. Certain religious attitudes or distortions of doctrine support this attitude while condemning alcohol. On the other hand, European and American countries have taboos towards drugs while accepting alcohol. For some distorted personalities, violation of these taboos affords an outlet for social hostility and satisfaction of need for guilt feelings not possible in " eastern cultures ".

Over the years, hypotheses have been advanced concerning the physiological factors in addiction. Some of these relate addiction to certain deficiencies or diatheses in neural and chemical mechanisms. Advocates of such theories feel that the " field theory " of human behavior is insufficient to explain drug addiction in many individuals. In this regard, the work of Hoffer et al.[1] proposing metabolic errors as an explanation for schizophrenia is of interest since this diagnosis is not uncommon in drug addicts. The " tranquilizing " drugs also offer possibilities of organic explanations, in addition to the environmental-psychological reasons for addiction.

Although we have spoken only of opiates at this point, one might well discuss hashish (marihuana), which is more commonly used in Mediterranean countries and also in Latin America, where it is not uncommon in rural areas to offer visiting friends a smoke of hashish as a " highball " is offered in other countries. Finding certain pleasurable sensations, the addiction-prone hashish smoker will seek a constant use to the detriment of himself as a useful citizen, husband or father. It has been hypothesized that he may be using it to negate his sexual anxiety or to heighten his sexual desire for a long-accustomed partner. On the other hand, and of etiological importance, is the fact that not all of his fellows smoke to abuse though they may all be poor, frustrated, and hungry. In this connexion it may be of interest to remember the statement of experienced Egyptian physicians that the cannabis drugs act like alcohol as far as sex is concerned; namely, to heighten the desire but inhibit the act.

In the western cultures, marihuana is a problem largely confined to certain social groups. Periodically, delinquently inclined groups of youths will take to smoking this drug. The dangers attendant on this activity are difficult to assess because of the many unsupported distorted stories of orgies which are a welter of confusion of fact and fiction. Aware of this, a number of youths are suspected of offering as an excuse for their delinquent acts the smoking of a few marihuana cigarettes.

The " why " of the use of a particular drug in a particular cultural or social setting is, if anything, less tangible than the reasons for drug use. Of probable significance are cost, availability, and custom, although certain ethnological mass psychological characteristics could play a part. The explanation of the varying use of heroin, morphine, the synthetics, and marihuana from time to time and place to place in the

[1] Hoffer, A., Osmund, H. & Smythies, J. (1954), *J. Ment. Sci.*, *100*, 29.

west is most difficult. One is tempted to formulate a concept of " psychic contagion ".

It would appear that the multifactorial determinants in the field of drug use make a clearly and easily defined approach to the problem exceedingly difficult. The lack of common cultural, religious, legal, and social denominators prevent easy generalizations.

Legal Framework for Treatment

The legal framework in which the addict is treated varies widely and seemingly without relation to culture or social attitudes. To trace the laws — written or unwritten — covering treatment is almost impossible in some countries. Much depends on the attitude of the enforcement personnel, public opinion of the drug addict, and the tolerance or lack of tolerance by the medical profession, to name a few of the obvious significant determinants.

Almost all the countries concerned with drug addiction and the treatment of the addict deal with them within the broad framework of the definition of legal use of narcotics, which is, briefly, for medical and scientific purposes only. The latter can be dismissed from consideration as their scope is fairly obvious. Medical use, on the other hand, has wide interpretation.

In the United States, for example, this is generally construed to include only the relief of pain and suffering incident to physical illness and not the satisfaction of addiction. Drugs may be used, however, in the withdrawal treatment of addicts, providing no supply is given to the patient and the treatment (with rare exceptions) is carried out in hospitals. Several European countries make a similar proscription against the support of addiction. Allowance is made for the person who (although otherwise physically fit) cannot be successfully withdrawn from drugs or who cannot make a satisfactory social adjustment with drugs.[2]

A number of states in the United States and several other countries provide for voluntary commitment under civil laws. These procedures are rarely used in most instances. There are civil procedures which allow for voluntary commitment but, because of civil rights in some countries, there is doubt of the validity of detention of patients under such laws.

Involuntary civil commitment is possible in 37 of 48 states in the United States[3] and in some European countries — for example, Germany — if the patient is dangerous to himself and others. It is used infrequently in these states although, at the same time, this method is more and more frequently recommended as a solution to the problem of treatment since it provides an unstigmatized long-term period of care and post-hospital supervision.

In essence, civil laws allow for an indefinite period of treatment in a hospital under the usual safeguards for medical records and disclosure of court records. Additional advantages include parole under conditions of supervision and treatment for long periods with the opportunity for the immediate re-hospitalization in case of relapse. However, once off drugs the addict may plead for release and, in many cases, achieve freedom. To complicate the problem further, the New York State Supreme Court has ruled, for instance, that the judge has no authority to commit an addict when there is no law against being an addict. Commitments under penal laws, on the other hand, are usually for definite periods (sentence), with limited conditions for experimental release (parole or probation), and the requirement of formal court proceedings for re-institutionalization in case of relapse. Commitments under penal laws do not, therefore, generally allow the kind of flexibility needed in treatment, nor do they provide the kind of medical treatment required.

Commitment under penal laws for treatment of addiction is accomplished in few countries. The United States has been the notable example since 1935, and constructed two special federal hospitals for that purpose, one at Lexington, Kentucky, and the other at Fort Worth, Texas. Iran provides camps in several provinces for this purpose, at which the addict stays for thirty days for withdrawal and re-education. Singapore also has recently developed such a treatment centre for addicts arrested and sentenced. Several other countries have planned, though not yet built, similar hospitals for the treatment of " criminally committed " addicts. An Egyptian law of 1928 makes such a provision as does a recent law in Greece. The majority of the countries, however, do not provide treatment facilities for convicted addicts.

An interesting combination of " criminal " and " civil " commitment has been developed in Washington, D.C., U.S.A., for addicts not under other criminal indictment. Under this procedure addicts may be forced to get treatment at a federal hospital and continue after-care follow-up in the city of Washington, D.C., for a period of two years.

Most countries recognize physical illness of any sort as justification for either special treatment or excuse from withdrawal treatment. The variations are so numerous and depend on so many diverse circumstances that it is impracticable to enumerate or explain them.

Programmes of Treatment

Although many countries have expressed an interest in the development of national programmes for the treatment of addicts, few have implemented their plans. Of these few, the United States and Iran have proceeded the farthest. Since 1935, the United States has had the two previously mentioned federally owned and operated hospitals for the treatment and rehabilitation of addicts. Several of the states — notably California and New York — have developed special in-patient facilities of a similar type. California opened a hospital in 1930 and closed it in 1940; the New York hospital was opened in 1952. In addition, a few large cities, such as Chicago, Illinois, and Detroit, Michigan, have special ambulatory psychiatric clinics for addicts for after-hospital care. Iran, in a special programme inaugurated in November 1955, established treatment centres in its several provinces to pro-

[2] *The Duties of Doctors and Dentists Under the Dangerous Drugs Act* (1956), Home Office, H.M.S.O.

[3] U.S. Council of State Governments Report 1954, E/CN.7/296 (April 1955).

vide withdrawal and short-term rehabilitation for addicts. In many countries — such as Germany, Denmark, and Argentina — addicts are treated in state mental hospitals when beds are available. In most countries, addicts can obtain treatment in either private sanatoria or on an ambulatory basis from private physicians.

Despite the rather general acceptance of the concept that drug addiction is but a symptom of an underlying psychiatric disorder, there is still a special focus on withdrawal techniques in treatment. As Kolb & Ossenfort[4] said in 1938, " The bulk of the literature on the treatment of drug addiction is concerned only with the withdrawal stage ... Some of these methods are harmful ... a large proportion are useless, and all are successful, provided the opiate is withdrawn and the treatment is not so strenuous as to kill the patient, a result that is too often achieved ". A comprehensive summary and discussion of such techniques has been made by Pablo Wolff.[5]

A brief outline of the principal methods of withdrawal and that plan which is currently considered the most scientific and humane may be useful.

There are generally two main categories : (1) The gradual withdrawal of narcotics over a period of time; (2) The abrupt cessation of the administration of narcotics with or without supportive non-narcotic drug or other therapeutic techniques.

1. The gradual withdrawal of narcotics can be divided into :

(*a*) The prolonged reduction with gradual diminution of the dosage of the drug of addiction over a period of weeks, months or even years. To ease the discomfort, adjunctive drugs such as barbiturates, bromides, scopolamine, atropine, hyocyamine, and more recently chlorpromazine, promazine, reserpine and meprobamate have been used.

(*b*) The rapid reduction in narcotic dosage over a period of seven to fourteen days. Supplemental therapy may include those in (*a*) above.

(*c*) The substitution of other addiction supporting narcotic drugs in (*b*) above, the withdrawal of which entails less severe symptoms than those encountered with the drug of addiction. This method used in the federal hospitals in the United States is as follows : the patient is given, depending on the severity of withdrawal signs and level of addiction, up to 20.0 mg of methadone (either orally or hypodermically) three times a day. After the first day the dosage is rapidly reduced to zero over a period of three to ten days.[6]

2. The methods of abrupt withdrawal include :

(*a*) Abrupt cessation of drug administration with or without supportive therapies such as intravenous fluids, cardiovascular stimulants in case of severe collapse.

(*b*) As above in 2 (*a*) and the use of adjunctive non-narcotic drugs as in 1 (*a*), such techniques usually only mask the symptoms of withdrawal.

(*c*) As above in 2 (*a*), except that electroshock or insulin shock is used periodically.

(*d*) " Patented " methods such as Démorphène which include a variety of drugs, the essential one of which is believed to be distearoglycerophosphate of choline.

However, there has been little scientific evaluation of most of these methods, and an over-emphasis on their respective efficacy in preventing relapse. A lack of understanding that addiction to drugs is but a symptom of the basic personality derangement is of paramount importance in this regard.

Most therapists treating addicts recognize the need for adjunctive and supportive treatment beyond somatic therapy. Reports from the literature in Europe and the United States lay repeated emphasis on the necessity of some form of psychotherapy to meet this need. Even the brief treatment programme accorded opium smokers in Iran recognizes the need to strengthen the ego and reinforce through persuasion, law enforcement, public pressure, etc., the knowledge of the bad effects of opium. In Egypt, those hospitals treating hashish smokers place great emphasis on group therapy. Reports from Germany emphasize that psychotherapy should be started at the beginning of treatment and maintained for weeks in the institutions and for months afterwards on an out-patient basis.

Unfortunately, the legal circumstances and opportunities for post-institutional treatment are unsatisfactory even in those countries with the most advanced health programmes. Except for addicts on parole or probation from criminal convictions, there is little opportunity even for post-institutional supervision, let alone treatment. Few, if any, public out-patient psychiatric clinics will handle addicts. In the United States, New York City has developed a combined in-patient and out-patient programme for juvenile addicts only under its public health laws. As previously mentioned, Washington, D.C., is about to provide similar services under " civil-criminal " commitment laws.

The question as to the kind of psychotherapy as well as additional therapies, vocational, occupational, etc., has been of greater interest in the United States than in most countries. There has been some experimentation with group therapy in United States government hospitals and the New York City Juvenile Addict Hospital (Riverside), and at the Abassia Hospital in Cairo, Egypt. Time-honoured individual therapies of the various types — e.g., supportive, psychoanalytic, and psychoanalytically oriented psychotherapy — are used by most therapists when such treatment is given. Countries with recognized problems of addiction among the unskilled and untrained have programmes of vocational education and re-education. Institutional treatment of any prolonged duration usually encompasses some form of occupational and recreational therapy.

Those addicts who are convicted of crime usually receive no special treatment, and are sent to prison as are other law

[4] Kolb, L. & Ossenfort, W. F. (1938), The Treatment of Drug Addicts at Lexington Hospital, *So. Med. J.* (Bgham., Ala.), *31*, 914.

[5] Wolff, P., The Treatment of Drug Addicts, *Bull. Hlth Org.*, (1945/46) L. of N., XII, No. 4.

[6] Vogel, V. H., Isbell, H. & Chapman, K. W. (1948), *J. Amer. Med. Assoc.*, *138*, 1019.

violators in their respective countries. In the United States and Iran, a few such criminals may be sent to special hospitals or institutions for treatment.

In Denmark, criminal addicts are often sent to the Institution for Criminal Psychopaths for treatment.

The use of N-allylnormorphine — which produces abstinence signs in narcotic addicts — has been suggested as a check method for relapse to addiction. This drug is dangerous in unskilled hands and if given incautiously to a heavily addicted person may produce so violent a reaction as to cause death. Furthermore, the test should be done in a hospital.

Certain countries as mentioned before provide for the continued use of drugs by individuals under controlled circumstances who have failed in attempted treatment. The lack of tight control over the licit dispensing of narcotic drugs in many countries makes possible the support of addiction with or without treatment. It is even possible, in many countries, for a physician to maintain an addict on drugs if he chooses under the guise of " medical treatment ". The frequency with which this occurs around the world is unknown but probably not inconsiderable, according to information from knowledgeable people in many nations. The individual economic resources to afford continued medical care made this possible in many cases.

Effect of Treatment

Few attempts to follow up large numbers of patients have been made. Thus, Pescor studied several hundred dischargees from the U.S. Public Health Service Hospital at Lexington, Kentucky, by correspondence. Unverified replies indicated that 15% of the patients had been off drugs for one or more years. About 50% of the inquiries were not answered. The U.S. Public Health Service is currently attempting methods to find by personal contact all patients discharged from Lexington in a large city. Efforts will be made to determine the addiction status as well. There will be no attempt to correlate results with treatment. A recent study on drug addicts in Vancouver, British Columbia, has been conducted by Stevenson. The results have not been published.

It has been suggested that addiction in some is but a temporary maturation problem, as in certain delinquent behaviour. Cursory reviews of United States prison statistics reveal the age of the majority of addicts to be in the third or fourth decade. Observers in Iran and Egypt are under the impression that not all young addicts become old addicts. Many of these implications titillate the imagination as to the possibility that drug addiction may be curable if only we had better information.

The identification of addicts both from relapse and epidemiological standpoints is of particular public health interest. Not only could such methods serve to evaluate treatment but also find those in need of treatment as well as determine the effectiveness of control procedures. A simple urine test would be invaluable. Present methods are time-consuming and cumbersome.

Future Needs

A great many questions which are of fundamental importance remain unanswered. We have too little information on the epidemiology of addiction, the fluctuations in incidence, the effect of cultural, legal, and social attitudes and taboos. There is, above all, little information on the effectiveness of any treatment programme to determine optimum methods of approach other than prohibition of drug use. The last, though undoubtedly effective, does not strike at the underlying problem of the desire for drugs and which results, despite the most stringent controls, in a certain number of people using drugs. Prevention is the watchword, but we must have more information in order to be wholly effective.

Abyssinian tea *(Catha edulis* Forssk, *Celastraceae)*

A study of some samples of varying geographical origin

By R. Paris, Professor, Faculty of Pharmacy, Paris, & Madame H. Moyse

Catha edulis Forssk belongs to the Celastraceae family and, a neighbouring species of the Evonymus, it is the sole representative of the genus *Catha*. The Swedish botanist Forsskal, the explorer of lower Egypt and Arabia, was the first to mention this plant, which he called *gat* or *khat*. His description of it was published posthumously in 1775 in his *Flora aegyptico-arabica* (8).

The plant has also been described under the following names : *Celastrus edulis* Vahl, *Catha forsskalii* Rich, and *Trigonotheca serrata* Hochst, *Methyscophyllum glaucum* Eckl. and Zeyher.

It is a shrub which grows to between 1-2 m in arid regions, and may reach 10 m or more in the equatorial zone; under cultivation, it may often grow to a height of 3-4 m. An evergreen in appearance, it is not unlike the spindle-tree. The leaves, which are bifarious — at least at the top of the branches — are whole, and lanceolate or ovate (8-10 cm long by 4-5 cm broad). The South African form (called *Methyscophyllum glaucum* Eckl. and Zeyher) is a variety with very narrow, bluey-green leaves (4.25 cm); they have a short petiole (0.5 cm) with two small caducous stipules. The limb, which at the base is smooth, has over the remainder of the leaf some thirty mossy serrations. The median vein projects on the underside and the secondary veins, running at an angle of forty-five degrees, meet in a curve near the margin of the limb. The leaves are coriaceous, smooth, shiny on the upper side, dark green when fresh, but becoming brownish or reddish-brown if kept; they have not much odour, but an aromatic, astringent taste. The flowers of type 5, arranged in axillary cymes, are small, regular in shape and greenish-white : they have a short calyx, petals longer, upright, overlapping, spreading out at the top, five alternisepalous stamens and free ovary with three loculi (Fig. 1). The fruit is a slightly trigonal, oblong capsule with three valves (Fig. 2), containing one to three seeds with a triangular, membranous wing. The albumen is pulpy and the cotyleda are foliaceous.

The anatomical characteristics of the leaf were described in 1893 by E. Collin (6). Their structure is fairly ordinary : prominent veins on the underside, glabrous epidermis, phlöem-lignous arc, pericyclic strands on the underside of the fascicule only, limb with asymmetrical, heterogeneous mesophyl with two palisade layers; twin crystals of calcium oxalate in the lower epidermis, under the palisade tissue and in the phlöem (3). A cross-section of the lower epidermis shows stomata, usually with three attached cells; the upper epidermis, without stomata, consists of cells with sinuate walls.

Geographical distribution. According to A. Chevalier (4), the plant originated in tropical East Africa. From Abyssinia, where khat grows wild along the river banks above 1500 m, it was introduced into the mountains in south Yemen and is also found in Kenya, Tanganyika, Uganda and South Africa (Transvaal, the Cape, Natal). It is cultivated in Abyssinia (in the Harar district) and in Arabia in irrigated terraces, and is often grown with the coffee plant at an altitude around 2,000 m. It is very hardy and can be grown in the Mediterranean region and in the south of the United States.

It is grown by sowing or from seedlings, and the leafy twigs are picked after three or four years. The drug is sold in bundles of stalks in full leaf weighing about 500 g and measuring 40 cm long by 8-10 cm in diameter. There are several varieties, differing in quality, the yellow leaves being the most sought after.

Chemical composition. The chemical study of khat goes back to the end of the nineteenth century; in 1887 by Flückiger and Gerock (7) who, in view of the stimulating properties of the drug, thought that it contained caffeine, discovered the presence of an alkaloid called *cathine*. Beitter, who wrote a thesis on it in 1900 (1), isolated an amorphous base, *katine*, the sulphate and hydrochlorate of which are obtained in crystalline form : the yield is low — 0.2% for leaves from Harar, 0.5% for those from Aden. In 1911, J. Chevalier obtained one per thousand total alkaloids (5) from the leaves; the content of the stalks would have been less. A little later, in 1912, Stockmann (22) separated three alkaloids which he called *cathine*, *cathinine* and *cathidine*, the first two in a crystal form; unfortunately, he gave no constants. He pointed out that, unlike cathinine, cathine and cathidine were fairly soluble in water. Cathine and cathinine can also be distinguished by their different solubility in pure alcohol, cathine sulphate being only soluble with difficulty in this solvent.

In 1933, Wolfes (24) undertook the extraction of khat alkaloid by benzine; after separation of cathidine, owing to its insolubility in water, he succeeded in obtaining cathine in a crystalline form (77°F.). The corresponding hydrochlorate, which crystallizes in pure alcohol after the addition of ether, melts at 181°F, its rotatory power being $(\alpha)^{20} = + 43.3°F$ (water); its ultimate analysis gives the formula $C_9H_{13}ON\ ClH$. Through these properties, the author showed that cathine is identical with d-nor-iso-ephedrine (or d-nor-pseudo-ephedrine), a substance found in its natural state in certain *Ephedras* in China (Smith (21)), and of which Nagai and Kanao made the synthesis with that of many derivatives of ephedrine (13). The formula of this substance is

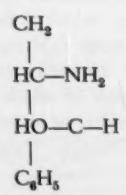

FIGURE 1

Twig of Catha edulis, *in bloom (Beitter)*

According to Manske (11), its constants are as follows :

Base, 77.5-78°F $(\alpha)_D^{20} = + 37.9°F$ (methanol)

Hydrochlorate, prisms 180-181°F $(\alpha)_D^{20} = + 43.2°F$ (water)

Sulphate, hexagonal flakes 295°F $(\alpha)_D^{20} = + 48.7°F$ (water)

As far as we are aware, no chemical study of the constitution of the khat alkaloid later than that of Wolfe's has been made.

Beitter (1), moreover, had noted the presence of mineral substances (11% ash), a tannin, a rubber-like substance similar to that of the *Celastrus*, glucides (manittol), and traces of essential oil. More recently, Plouvier (20) identified dulcitol, as with various other *Celastraceae*. Mustard (12) determined the ascorbic acid content, which is fairly high in the leaves (324 mg — 100 g) and twigs (138 mg — 100 g), and which perhaps plays a role in the tonic action of the drug (25). As to cholein, the presence of which is indicated in certain *materia medica* works, there seems to have been confusion with *Caltha palustris* (cf. E. Paulsen, *Tidsk. Kem. Farm. Terap.*, 1916, 13, 237 and 262).

Use and Physiological Action

Khat leaves have been long used by the Arabs and Egyptians in order to overcome fatigue and sleep. Although there is no proof that its use goes back to classical antiquity, according to Leloup (10), it was known before coffee, and it was mentioned in the fifteenth century. Its main use is for chewing, and in the Yemen it was the custom to offer it to visitors, each guest, after chewing the leaves, throwing the remains with the stalks on the ground (2). Khat chewers are thus able to dance and talk all night without feeling sleepy, both fatigue and hunger being eliminated; the drug also seems to be anaphrodisiac (10). With a slightly astringent taste, khat also makes a very agreeable tea (*khat* is the leaf and *kafta* the beverage) in the proportion of 5-15 g per litre. According to Greenway (9), it is also used in South Africa as a stimulant and as a remedy against diseases of the chest.

The fresh drug is always preferred to the dry plant, which is considered to have lost part of its effectiveness. Continued use of khat leads to addiction, and in the long run khat chewers may become auto-intoxicated, the drug inducing a state of stupor, hebetude, changes of character and incapacity

FIGURE 2

Twig of Catha edulis, *with fruit (Beitter)*

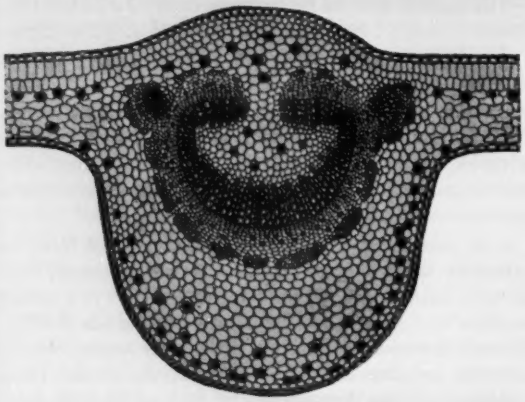

FIGURE 3

Cross section of the Catha edulis *lea, at the median vein (E. Colin)*

for work. Greenway (9) reports some cases of madness and one case of poisoning. In addition to nervous diseases and heart trouble, the after-effects include gastritis, constipation and emaciation.

With the exception of certain clinical tests by Leloup (10) showing the beneficial effects of khat in cases of asthenia and overwork, the first physiological tests were made by Beitter (1), who noted only a temporary paralysis in frogs after large doses of "*katine*". But it was J. Chevalier (5) who made the first major experiments with cathine (the raw alkaloid, for which he does not give any constants) on different animals — frogs, guinea pigs and rabbits. This substance is not very toxic; after a period of hyper-excitation it induces muscular relaxation, motivity is gradually reduced, the heart slows down and, with heavy doses (0.01 g per frog) stops on the systole. With guinea pigs and rabbits, after intravenous injection of doses of 0.3-0.4 g, there was lack of motor co-ordination and convulsions followed by paralysis.

In 1912, Stockmann (23) studied separately the action of the different alkaloids that he had isolated. Cathine appeared to act both on the nervous system and on the muscles, cathinine having a less depressive effect on the encephalon, but being more stimulating to the medulla; cathidine seemed to be mainly a muscular poison but, being insoluble in water, would hardly affect the action of the drug, at least when taken as a tea. In 1942, Brücke (3) studied the action of pure cathine sulphate (d-nor-pseudo-ephedrine), the only clearly defined alkaloid of khat. He was particularly interested in its stimulating action on the central nervous system, which he studied in mice, noting the degree of excitation. In particular, he compared the action of cathine with that of pervitine; whereas the latter produced excitation in mice with a dose of 1 α/gr, doses a hundred times stronger of pure cathine sulphate (sub-cutaneous injection) were necessary. The l-ephedrine had an action similar to that of cathine, the d-pseudo-ephedrine having no excitant effect with an almost fatal dose. The effect of cathine on the blood pressure of a decapitated cat was one thousand times less marked than that of adrenalin, and its action was weaker than that of ephedrine; the high blood pressure induced was lasting. The author concluded that the weak stimulating action of cathine on the nervous system, given the content of this alkaloid in the drug, cannot be the cause of the stimulating effect of the fresh plant. He considered that, at least in fresh khat, there must be some other active principle of the benzedrine type — the formula for which, very similar to that of cathine, is only one oxydril less. That, however, is merely a hypothesis.

Therapeutic Indications

Although earlier writers such as Dujardin Beaumetz, Leloup (10) and later J. Chevalier (5) recommended it as a general stimulant and mental excitant, khat appears to have been used only rarely in European medicine (25). The 1949 British Pharmaceutical Codex lists it only as a substitute or adulterant of tea.

PERSONAL RESEARCH

In view of recent French legislation on khat and having had available several samples of the drug, we have endea-

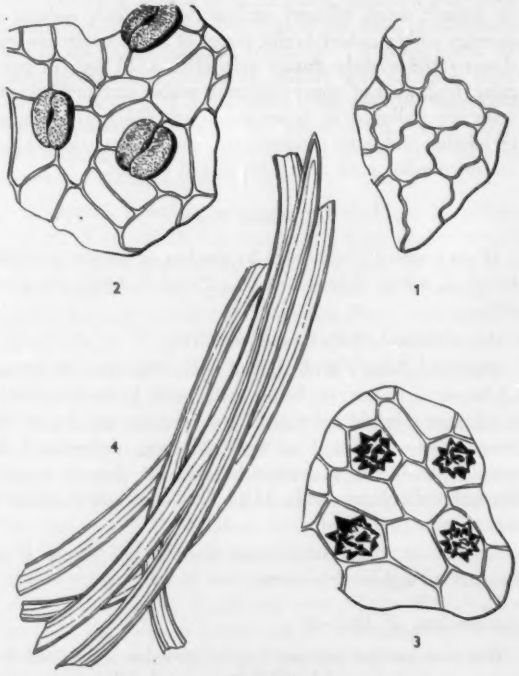

FIGURE 4

Characteristic elements of Catha edulis *powder*

1. Upper epidermis, front view
2. Lower epidermis, front view
3. Oxiliferous cells
4. Pericyclic stran[illegible]

voured to determine its characteristics (16). This has entailed the definition of some of its chemical and physiological properties.

Samples Studied

Parcel 1 : Leaves of Ethiopian khat; an old sample kept in the *Materia medica* Museum of the Faculty of Pharmacy, Paris.

Parcel 2 : Leaves of Amani (Tanganyika) khat, picked in 1949, by the courtesy of Mr. P. J. Greenway, Systematic Botanist.

Parcel 3 : Fresh twigs of *Catha edulis*, picked in 1957 at the Botanical and Phytopathological Station of the Villa Thuret, Antibes, Alpes Maritimes (Director : Mr. J. Barthelet).

Parcel 4 : Fresh twigs of *Catha edulis*, picked in July 1957 in the garden of the French Faculty of Medicine and Pharmacy, at Beirut, by Professor B. Lys.

Botanical Test

The whole leaves of khat are fairly easily recognizable by their general morphological and anatomical characteristics (Figs. 1, 2 and 3).

The *powder* can be identified under the microscope, after clarifying with chloral or potassium, by the following elements : many strands isolated or in groups, colourless, tapering, with narrow lumen (Fig. 4 (4); remains of ducts, streaked or dotted; small, calcium oxalate twin crystals isolated or in series within uniserial cells; pieces of lower epidermis with stomata and slightly sinuate cells (Fig. 4 (2)) and, in particular, fragments of upper epidermis whose extremely sinuate walls are scalloped in appearance (Fig. 4 (1)). The absence of sclerites and hairs eliminate tea, and in mate the stomata are surrounded with cells with striped cuticles.

Chemical Test

Water content : Determined by the loss of weight at 100°F; Parcel 1, 8.4%; Parcel 2, 9.2%; Parcel 3, 66%; Parcel 4, 60%.

Ash : Parcel 1, 9.4%; Parcel 2, 7.95%.

Data on infusion : With diluted ferric-chloride, it is greenish-brown in colour; on being boiled with hydrochloric acid it takes on a bright red tinge. These reactions are due to the presence of catechuical tannins and were determined, in sample No. 2, by precipitation with the Stiasny reagent (formol-hydrochloric acid), 14%. The foam colour index is approximately 100.

Essential oil : Steam distillation showed only traces of an essential oil lighter than water.

Determination of Alkaloids

This was carried out on 5 g of powder alkalinized by sodium carbonate and extracted, hot, by chloroform. The organic liquid was treated with diluted hydrochloric acid; after alkalinization by ammonia, the aqueous solutions were extracted by ether-chloroform (3-1 by volume), which was evaporated and dried.

This method gave the following contents : Parcel 1, 0.17%; Parcel 2, 0.18%; Parcel 3, 0.18%; Parcel 4, 0.2% (figures reduced to the dried plant and therefore constant in the different parcels).

By cold maceration, the figures obtained were much lower. Moreover, since certain alkaloids are soluble in water, it is advisable to undertake a kind of salting out by sodium chloride or ammonium sulphate when the alkaline aqueous solutions are extracted by ether-chloroform.

In an attempt to obtain alkaloids in crystallized form, an extraction was attempted, using a Soxhlet apparatus, with 250 g of leaves of parcel No. 2. Petroleum ether in a neutral medium carried off a small quantity of alkaloids (0.02%). After alkalinization by ammonia, the powder was successively extracted by ether and by chloroform, the process being continued as in the determination of the total alkaloids, with a resulting residue of 0.08% for ether and 0.03% for chloroform. The total yield was therefore 0.11%.

Extraction by lixiviation by means of a 3% concentration of acetic alcohol, displacement of bases by sodium carbonate and extraction by the ether-chloroform mixture, gave a lower yield of 0.07%.

The total alkaloids gave the reaction of iodoform with iodine in an alkaline medium; with a 10% concentration of copper sulphate and with soda, a blue-green precipitate insoluble in ether was obtained. A portion of the bases being dissolved in a few millilitres of pure alcohol, sulphuric acid was added until a definitely acid reaction was obtained and then, after a few drops of ether, white crystals, recovered by centrifuging and washed in pure alcohol, appeared fairly quickly (particularly if left for a few hours in a refrigerator). The fusion point (instantaneous) was 298°F (decomposition), showing that this was cathine sulphate (d-nor-iso-ephedrine). Also, by dissolving another portion in a small quantity of alcohol containing hydrochloric acid at 5% and the addition of anhydrous ether, a hydrochlorate was obtained with a fusion point (178°F, instantaneous) corresponding to that of cathine hydrochlorate.

Finally, in the analysis of khat and its preparations, paper chromatography and electrophoresis were used, both methods having been already applied by various authors and by ourselves (14, 15, 17) for various medicinal plants.

Using paper chromatography, we tried one-fifth and one-half tinctures, an equal weight of fluid extract, and total alkaloids. We used an ascending chromatography at a temperature of 18° ± 1°, on *Arches* 301 paper, aqueous butanol, acetic butanol (4, 5, 1) or the mixture petroleum ether (B.P. 80°F), amylic alcohol, acetic acid, water (1, 3, 3, 3). As detectors, the Dragendorff reagent (based on Munier's formula) and ninhydrine (0.2% solution in alcohol at 80°F) were used. Ferric perchloride and potassium were used also with the tinctures and the fluid extract, giving from the starting line a very elongated spot on the first third of the chromatogram, corresponding to the tannins. With the one-half tincture and ninhydrine, a rather dull, violet-rose spot (Rf approximately 0.5 in aqueous butanol) was obtained. With the same detector and the fluid extract six clear spots were

obtained (in acetic butanol); with Rf 0.11, 0.17, 0.25, 0.28, 0.38 and 0.68, the first three and the last being violet-rose in colour and the other two yellowish.

The total alkaloids were compared with ephedrine (a 2% solution of tevogyne ephedrine hydrochlorate). This base, which showed no fluorescence in ultra-violet rays, was practically insensitive to the Dragendorff reagent (0.1 mg per sampling test was required in order to obtain a clearly defined spot), but reacted better to ninhydrine (20-40γ), giving a violet-rose spot.

This method showed the presence of three alkaloids in khat (sampling test 0.1-0.2 mg of total bases). The first two bases, not revealed by Wood's light or by the Dragendorff reagent under these conditions, gave violet-rose spots in ninhydrine with Rf values approximating to that of ephedrine. The third base, fluorescent, greenish yellow in ultra-violet rays, did not appear after detection by the Dragendorff reagent, and its Rf was much higher :

Solvent	Ephedrine (levogyrous)	Rf of khat alkaloids		
		Base No. 1	Base No. 2	Base No. 3
Aqueous butanol	0.52	0.48	0.57	0.92
Acetic butanol (Partridge's mixture)	0.69	0.63	0.72	0.95
Petroleum ether—iso-amylic alcohol—acetic acid-water (1, 3, 3, 3)	0.75	0.72	0.78	0.95

As regards caffeine, this cannot possibly be confused with the khat alkaloids : it showed no colouring under ultra-violet rays or in ninhydrine, and was only detected by the Dragendorff reagent (Rf 0.68 by acetic butanol and 0.62 by the petroleum ether-iso-amylic alcohol-acetic acid-water mixture).

With paper electrophoresis, using the Macheboeuf apparatus and formic acid 2N (pH 1.5), with the total alkaloids (10 mm³ of an 8% solution), in 2½ hours several spots appeared fluorescent under ultra-violet rays (2 greenish yellow, travelling very little, and 2 blue). After soaking in the Dragendorff reagent, levogyrous ephedrine (2.5 mm³ of a 2% solution) gave a violet spot. The total alkaloids of khat gave 5 orange-red spots, some having travelled a little, others more or less the same or farther than ephedrine. These results suggest a greater complexity of the alkaloid composition of khat.

Physiological Tests

Using the four samples studied, experiments were made on mice by subcutaneous injection with :

One-fifth tinctures in alcohol at 60% were prepared by maceration with dry samples of the first two parcels. Just before use, these tinctures were half evaporated and made up to the original volume with distilled water. The fresh drugs (parcels 3 and 4) were stabilized with boiling ethyl alcohol, and, after drying and pulverization, extracted by boiling, using the same solvent. The alcohol was then re-distilled dry under reduced pressure and the residue recovered using a weight of boiling water corresponding to the weight of the drug used.

Toxicity for mice (sub-cutaneous injection)

Parcel No. 1 : For a dose corresponding to 10 g of dried plant per kg, only temporary muscular relaxation was observed and mortality was only 10%.

It should be added that with the same dose and under the same conditions, preparations of dried tea leaves produced a mortality of 20% and those of maté 100%.

Parcel No. 2 : With a dose of 5 g/kg of dried drug there was good tolerance. With 7.5 g/kg, there was a brief period of agitation with cardiac and respiratory acceleration and pedalling movements with the hind legs, followed by torpor and muscular relaxation : Mortality, 20%.

With 10 g/kg, the stage of excitation was less clearly defined and the oncoming of torpor more rapid : 60% deaths in 48 hours.

Parcel No. 3 : The dose of 10 g of fresh plant per kg (corresponding to 3.3 g of dried plant) produced no reaction. With 4 g/kg (dried plant), agitation was observed. With 7.6 g/kg (dried plant) there were phenomena of paralysis and in the following few days mortality was 40%.

Parcel No. 4 : After the dose of 10 g of fresh plant per kg (corresponding to 4 g of dried plant), pedalling movements with the hind legs were observed in one-third of the animals and in the others muscular relaxation : Mortality was 30% after 24 hours, 40% after 48 hours; with 25 g/kg (corresponding to 10 g of dried plant) there were the same observations (immediately after the injection mice were panting and making pedalling movements with the hind legs) and mortality was 80% after 24 hours.

It appears, therefore, as already pointed out by different authors (3, 10, 18, 19, 23), that for the same alkaloid content, the fresh plant is definitely more toxic than the dried plant. Total alkaloids were tried with a dose of 50 mg/kg and under the same conditions. With this dose — corresponding practically to 40 g of dried leaves, there was only a short stage of excitation, which was not followed by torpor or death.

The whole plant is thus relatively more toxic, particularly when fresh, than the isolated total alkaloids, which seem to represent only a part of the physiological action. It should be noted that a tincture obtained from a powder from which the majority of the alkaloids have been extracted by ether-chloroform in an ammonia medium still possesses a toxicity almost equal to that of the untreated drug. To sum up, we examined four samples of different origins (from Ethiopia, Tanganyika, the south of France and the Lebanon, the two latter being fresh), and found their total alkaloid content (compared with the dried drug) appreciably the same. Paper chromatography of the latter may be useful in the analysis of the drug. The high toxicity in sub-cutaneous injection, which is relatively higher in the case of the fresh samples, does not seem to be due solely to the alkaloids.

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Prevention of narcotics offences

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The Federal Criminal Bureau, Wiesbaden, held a conference on " The Prevention of Narcotics Offences " from 21 to 26 November 1955. Invitations to the conference were sent to representatives of all districts engaged either in the prevention of narcotic offences (Special Duty Officers of the Criminal Department) or in the supervision of the legal trade in drugs (Federal Opium Bureau, Boards of Health).

Statements dealing with the whole problem of narcotics traffic and addiction were delivered by experts in each of the various aspects. These statements have been published by the Federal Criminal Bureau in a volume with the title " Bekämpfung von Rauschgiftdelikten " * (Fight against Narcotics Offences). They are summarized below.

In his introductory paper, Dr. Niggemeyer (Regierungsdirektor in the Federal Criminal Bureau) refers briefly to the nexus of problems bound up with drug addiction and the criminal offences to which it gives rise. He lays special stress on prevention — i.e., protection of the citizen against addiction — and goes on to point out that what is wanted is not so much fresh legislation as the full enforcement of existing possibilities. The prevention of narcotics addiction spells the prevention of crime. The strict observance of the regulations for the prescription and supply of narcotics, as contained in the German opium law, impedes the spread of addiction and so of a grave danger to the life of the individual citizen, a danger which the latter is unable to recognize. It also safeguards the State against serious social evils.

Mr. Leichtweiss (Kriminalrat in the Federal Criminal Bureau) offers a historical survey of the use of narcotics for religious and medical purposes from the earliest times. He states that narcotics were used to cause or prevent certain physical conditions (to increase energy, or overcome hunger, thirst or fatigue).

Particular mention is made of the historical development of the enjoyment and use of opium, hashish and coca leaves.

1. The use of opium as an analgesic drug was known to the Sumerians from about 3000 B.C. onwards. The smoking of opium (with or without tobacco) was introduced in the seventeenth century.

2. Hashish was also known in the pre-Christian era in Mesopotamia as a vehicle of visionary dreams. Its medical use is not mentioned. Indian hemp first reached South and Central America in 1545, and became known there as a narcotic under the name of marihuana.

3. Cocaine leaves were used by the Incas as a stimulant in prehistoric times.

Among narcotics — e.g., betel and peyotl — reference is made to " wake-amine ".

In his last paragraph, the author quotes from Baudelaire's *Les paradis artificiels :*

" Were there a Government minded to destroy its subjects, it would only need to encourage them to take to hashish " and he continues :

" We can go further and say without any exaggeration that a Government exposes its people to the gravest dangers if it does not do its utmost to check the abuse of narcotics or at least to restrict it to an unavoidable minimum."

Dr. A. Spaich (Board of Health, Stuttgart) takes for his theme " The Task of the Board of Health in the Prevention of Narcotics Addiction and Treatment of Addicts ".

Under the official regulations the care of addicts is the responsibility of the boards of health. Accordingly, the medical officers' duties, where the prevention of narcotics addiction is concerned, include the detection, treatment and after-care of addicts.

The detection of each and every addict is difficult enough in itself. It demands the co-operation of pharmacists, local practitioners, hospital doctors, sickness funds and the special duty criminal police officers engaged on drug-addiction.

According to the findings of the Stuttgart Board of Health, about 20% of addicts are doctors, and 33.2% belong to one branch or another of the medical profession.

As regards the total number of addicts, the author draws attention to the following important facts :

" It cannot be denied that some doctors are unfortunately very liberal in supplying drugs, particularly when they themselves are addicts."

Many examples are then given of the doings and treatment of addicts. Voluntary withdrawal cures are described as highly problematical and ephemeral; most of them too short. The treatment of medical addicts is referred to as a special case.

One valuable point made by the author is " that the origin of the addiction may often be accompanied by adverse material circumstances and difficulties which act as a stimulus. Special care should therefore be taken to see that on discharge from the withdrawal cure the addict returns to suitable conditions at home and is immediately re-integrated into employment ".

Dr. Becker, a pharmacist of Wiesbaden, explains the regulations governing the dispensing of narcotics in pharmacies. The pharmacist must check the prescription as to both form and content. He must only dispense it if correct. A pharmacist cannot often come to a decision as to whether a pre-

* *Bekämpfung von Rauschgiftdelikten*, Bundeskriminalamt, Wiesbaden, 1956, 200 pp.

scription is " medically justified ", but he will expose himself to prosecution " if he dispenses narcotics although aware that the doctor has committed a breach of the rules of medical practice by prescribing improperly or without due care ".

The pharmacist must enter in the register every sale showing the description and amount of the drug and must keep for five years all prescriptions not made out for the account of a recognized sickness fund. The delivery of supplies to pharmacists by a manufacturer or wholesaler requires a permit from the Federal Opium Bureau.

The Head of the Federal Opium Bureau, Dr. Gewehr, of Coblenz, dealing with " The Legal Basis of the Federal Opium Board and its Task " states :

> " No operation of any kind connected with narcotic drugs (import, export, manufacture, wholesale distribution) is lawful unless authorized by the Federal Opium Bureau and every transaction in narcotic drugs requires a separate permit, valid for that transaction only. The Federal Opium Bureau is kept constantly informed of the total consumption of narcotic drugs by means of regular returns made by all permit-holders and pharmacists who dispense the drugs to consumers on medical prescription."

Mr. Eschenbach (Kriminalrat in the Federal Criminal Bureau, Wiesbaden) has a particularly interesting contribution on " Types of Narcotic Delinquency ". The author gives many examples of typical narcotic offences drawn from actual cases. Without going into these in detail, we may summarise some of his basic arguments as follows :

" Persons who have fallen a prey to narcotics or similar drugs are bound, sooner or later, to lead a life outside the law, since they can only procure the addiction-forming drugs illegally. Understandably, therefore, the police officer is bound to adopt towards the addict who has turned to crime and whom the officer encounters as swindler, forger and thief, constantly on the move and always relapsing into wrong-doing, a more stringent and ruthless attitude than does the doctor, who regards the addict, even when he is acting against the law, merely as a patient in need of help and protection.

" But the doctor and the police officer are united in their aim, for there is the ever-present danger that where the law is not enforced and the regulations as to supervision are not strictly applied addiction will lead to a flood of delinquency.

" The causes which make an addict a criminal and an habitual offender are in part different from and more compelling than those affecting other groups of wrong-doers.

" Addicts become listless and unstable, unreliable, conceited, shallow and indifferent to family and job. Their whole thought centres on obtaining the drug. Their powers of restraint and of decision are so weakened that they become unpredictable and potentially dangerous.

" The change brought about by the poisoning of the addict's mental and spiritual make-up leads inevitably to the complete subordination of all social and moral considerations to the anxiety to procure the drugs. The sense of social responsibility disappears; the addict becomes asocial.

" A high percentage of addicts are doctors and nurses. This is an alarming fact, since medical personnel are responsible for the welfare of the patients committed to their care. Addicts have a considerably diminished moral sense, capacity for judgment, power of decision and sense of responsibility. The neglect of due professional care in the treatment of patients, especially in surgical cases, is a grave danger to the community. Medical addicts are more prone than practitioners who have not succumbed to addiction to prescribe drugs in unsuitable cases.

" There is therefore every reason for demanding that a close watch be kept on medical personnel. Leniency and indulgence are out of place in the case of medical addicts."

Mr. Eschenbach concludes as follows :

" Thus addicts, until finally cured, represent a constant danger to the community. It is a danger which forces the legislator to pass stringent laws and causes those concerned with the prevention of addiction and crimes of addiction — doctors and pharmacists, the courts, the administrative authorities and the criminal police — to make sure by close co-operation that the laws and regulations are observed with strict exactitude and that all transgressors are detected and duly sentenced for their own safety and reformation."

Another important and interesting subject is the legal position with regard to the institutionalization of convicted addicts. Mr. Asbrock, Kriminal Kommissar in the Land Criminal Bureau, Lower Saxony, deals with the possibility of placing convicted addicts in institutions practising the withdrawal cure or sanatoria.

Institutionalization is of two kinds : penal and administrative.

Penal Institutionalization

Under section 42 b of the Penal Code persons, whether completely irresponsible or of diminished responsibility, can be placed in a sanatorium.

This section can only be applied when a punishable offence has been committed. Convicted addicts who have been sentenced for a crime or misdemeanour committed under the influence of drugs, can, under section 42 c of the Penal Code, be placed in an institution practising the withdrawal cure.

Administrative Institutionalization

In Lower Saxony, the compulsory institutionalization of mentally affected addicts is made possible by the Law on Public Safety and Order of 21 March 1951. Under section 9 of this law, both the administrative and the police authorities can take persons into custody if this is necessary : (1) for their own protection; or (2) in order to quell a disturbance of public safety and order or prevent an imminent danger to public safety and order.

The words " prevent an imminent danger " may be taken as including prevention of a criminal offence. Every narcotic addict whether or not under the influence of a narcotic drug constitutes a danger in this sense.

The titles of the other statements delivered at the conference are :

The chemistry and pharmacology of narcotic and similar drugs

Psycho-pathology of addiction with particular reference to drug addiction

The work of the Commission on Narcotic Drugs of the Economic and Social Council of the United Nations

Experiments by the police in dealing with criminal drug addicts in Berlin

Narcotic drugs criminal law

The institutionalization of drug addicts outside the purview of the criminal prosecution authorities

Co-operation of the Court doctor with the police, public prosecutor and Court in the prevention of narcotic offences

Narcotics offences in the international field (the legal position, organizations, conventions, the illegal narcotic drugs traffic) International narcotics smugglers

Narcotics delinquency as reflected in the police statistics — general rules for the treatment of reports of narcotics offences (police registration)

Current problems of the prevention of drug addiction in medical practice.

Dr. Alfred Sao-Ke SZE

In January 1958 Dr. Alfred Sao-Ke Sze died in Washington, D.C. During his long life he showed continuous and positive interest in the development of the international community, and in particular played an important part in the development of international narcotics control : he represented China at the two opium conferences held in Geneva in 1924 and 1925, which resulted in the opium smoking agreement of 11 February 1925 and in the International Drugs (Opium) Convention of 19 February 1925. Although China did not become a party to these treaties because they did not go far enough, it is largely due to the firm position Dr. Sze took that the Convention became a more satisfactory basis for the existing system of international narcotics control.

Dr. Sze was born at Cheng-tzeh, Kiangsu, China, on 10 April 1877, and he was one of the few Chinese students to go to the United States in the days of Imperial China in order to continue his education. At sixteen he entered Central High School in Washington, D.C., and then Cornell University, where he obtained his B.A. in 1901 and his M.A. in 1902. He was later awarded honorary degrees by various universities.

After returning to China he passed the imperial examinations and entered the Chinese Civil Service.

He started work in the field of communications, being Director of the Northern Railway in 1908. In 1911, the Chinese Republic made him its first Minister of Posts and Communications. From then on he continuously held important posts in high government circles, being Minister to the United Kingdom from 1914 to 1921; to Washington from 1921 to 1929; to the United Kingdom again from 1929 to 1932; and to Washington again from 1932 to 1937. He was Minister of Foreign Affairs in 1923.

In the international field he also filled a variety of important assignments : delegate in 1918 at the Peace Conference in Paris; in 1921 head of the Chinese Delegation to the Washington Conference; head of his country's delegation at the Twelfth Assembly of the League in 1931 when China was elected to the Council of the League. In this capacity he showed extreme skill in the handling of the Chinese case at the time of the invasion of Manchuria.

Retiring from the diplomatic service in 1937 he made his home in Shanghai where he engaged in charitable activities but continued to serve his Government in an advisory capacity. During and after the Second World War he showed his extreme vitality by working again, especially as Senior Advisor to the Chinese Delegation to the San Francisco Conference, then as an Advisory Counsellor of the World Bank from 1947 to 1950, and by various other important missions.

In the words of the Chinese sage, his life was a quiet river which brought about rich crops. The Editors of the *Bulletin on Narcotics* wish to extend heartfelt condolences to Doctor Sze's family.

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SCIENTIFIC PUBLICATIONS ON NARCOTIC DRUGS FOR 1957

Introduction

The following bibliography has been prepared by the Secretariat and includes scientific publications on narcotic drugs which appeared during 1957, as well as a few which appeared earlier but could not, for various technical reasons, be included in the preceding lists published in the *Bulletin on Narcotics*. This bibliography makes no claim to be complete, and information regarding books or articles not included in it would be gratefully received by the Division of Narcotic Drugs, European Office of the United Nations, Geneva, Switzerland.

The bibliography has been arranged by subject in the following way :

Part I. General works

Part II. Opium poppy, opium and drugs manufactured therefrom

- A. Opium poppy, opium and opium alkaloids collectively considered
- B. Morphine
- C. Other phenanthrene alkaloids and derivatives of opium
- D. Other drugs and substances derived from the opium poppy

Part III. The coca leaf and cocaine

Part IV. Cannabis and its derivatives

Part V. Synthetic drugs

- A. General works
- B. Pethidine and related compounds
- C. Methadone and related compounds
- D. Morphinan and morphine synthesis

Part VI. Addiction to narcotic drugs

Part VII. Miscellaneous

Under each heading, publications are arranged alphabetically by author. Owing to the nature of the sources available to the Secretariat for preparing this bibliography, several titles are given in translation only. They are preceded by an asterisk.

The bibliography is now prepared for both English and French editions; therefore translations in both languages follow those titles which are not in one of the working languages.

Part I. GENERAL WORKS — GÉNÉRALITÉS

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Part II. OPIUM POPPY, OPIUM AND DRUGS MANUFACTURED THEREFROM — PAVOT A OPIUM, OPIUM ET DROGUES QUI EN SONT TIRÉES

A. Opium poppy, opium and opium alkaloids collectively considered — Pavot à opium, opium et alcaloïdes de l'opium considérés dans leur ensemble

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